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Polygonum minus: A tropical medicinal herb with vast applications in food, agricultural, and medicinal fields

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ABSTRACT

Polygonum minus (PM) is a tropical medicinal herb that belongs to the family Polygonaceae, widely distributed in Southeast Asia, such as Malaysia, Indonesia, and Thailand. This herb has a sweet and pleasant aroma, commonly used as a flavoring agent. In addition, it is applied as a traditional medicine for multiple diseases, such as fungal infections, poor eyesight, and body aches. Due to its antioxidant and antimicrobial properties, PM is employed as a food additive for delaying or preventing the oxidation reaction of food and as an edible film for protecting food from microbiological contaminants. In livestock, poultry, and aquaculture industries, PM has been proposed as an alternative to traditional growth promoters with anti-parasitic properties. In respect of medicinal applications, PM has been proven to have protective effects on body systems and inhibitory effects on microbes. Moreover, nanotechnology has been applied to improve the efficacy and bioavailability of PM. This review aims to provide insight into the traditional uses, phytochemical properties, and toxicity, as well as applications of PM in food, agricultural, and medicinal fields.

1. Introduction

Polygonum minus (PM) is an annual medicinal herb (Huda-Faujan, Noriham, Norrakiah, & Babji, 2009; Murakami, Ali, Mat-Salleh, Koshimizu, & Ohigashi, 2000) that belongs to the family Polygonaceae (Rahnamaie-Tajadod, Loke, Goh, & Noor, 2017), with sweet and pleasant aroma (Baradaran, HooiLing, ChinChin, & Rahim, 2012). It is a slender, creeping shrub and can reach up to a height of 1.0 m in the lowlands and up to 1.5 m in the highlands (Vikram, Chiruvella, Ripain, & Arifullah, 2014). The stem is a slender twining shrub; its leaves are long and lance-shaped, 5–7 cm long and 0.5–2.0 cm wide. Moreover, the stem is cylindrical, green, and slightly reddish, while the internodes are short with nodes (P. V. Christapher et al., 2015). The morphology of PM is shown in Fig. 1. Furthermore, PM is widely distributed in Europe (Narasimhulu & Mohamed, 2014) such as Britain, Scandinavia, Spain (Bunawan, Talip, & Noor, 2011), and Southeast Asian (Gattuso, 2001; Udani, George, Musthapa, Pakdaman, & Abas, 2014) such as Malaysia (Qader, Ameen Abdulla, Chua, & Hamdan, 2012), Indonesia (Rusdi, Goh, & Baharum, 2016), Thailand (Vikram et al., 2014; Zakaria, Baba, Ku Bahaudin, & Hamdana, 2015), Vietnam (Rusdi et al., 2016), Laos (Ahmad et al., 2014), and Sri Lanka (Panase & Tipdacho, 2018). Fig. 2 shows the main distribution areas of PM in the world. PM, as synonyms to *Polygonum kawagoeanum*, *Persicaria minor* (Bunawan, Choong, Md-Zain, Baharum, & Noor, 2011), and *Persicaria tenella* (Chia et al.,

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2020), is called as Pygmy smartweed/knotweed in English (Burkill, 1966; Malaysia Biodiversity Information System (MyBIS)), kesum in Malaysia (Aziman, Abdullah, Mohd Noor, Zulkifli, & Wan Kamarudin, 2012; Johnny, Yusuf, & Nulit, 2011; Mohd Ghazali, Al-Naqeb, Krishnan Selvarajan, Hazizul Hasan, & Adam, 2014; Roslan et al., 2012; Shukor, Ismail, Zainal, & Noor, 2013), daun laksa in Singapore (Vimala, Rohana, Rashih, & M, 2011), phakphai in Thailand (Vikram et al., 2014), Kleiner Knöterich in German, Chakhong-macha in Manipuri, and Nghể bé in Vietnamese (P. V. Christapher, Parasuraman, Asmawi, & Murugaiyah, 2017). Additionally, PM has various vernacular names such as kesom (Imelda, Faridah, & Kusumaningrum, 2014), laksa leaves (Abas, Lajis, Israf, Khozirah, & Kalsom, 2006; Noor Hashim, Abas, Shaari, & Lajis, 2012), kusum (Bashir, Aziz, & Noor, 2020), daun laksa or cenohom (Ong & Nordiana, 1999), Jarak Belanda, Kunyit Jawa, Kelima Paya (Qader et al., 2011), cambodian mint, vietnamese mint, water pepper, and marsh pepper (Hamid et al., 2020).

The extensive use of PM, particularly in food and traditional medicinal fields, has attracted the attention of researchers, and various review studies have reported the phytochemical constituents, medicinal properties, or bioactive properties of PM (Asanai, Haron, Camalxaman, & Mohamed, 2020; Nadzirah, Rusop, & Noriham, 2014; Narasimhulu, Reddy, & Mohamed, 2014; Paritalac et al., 2014). However, few researchers have attempted to review the application progress of PM in various fields in recent years. Therefore, the current knowledge about the food, agricultural, and medicinal field applications of PM is reviewed in this article. In addition, we put forward the issues that need to be resolved in future investigations, which is meaningful for broadening PM applications.

2. Phytochemical

2.1. Phytochemical compositions

The diverse chemical constituents present in medicinal plants possess biological attributes that could improve human health through applications in the food and pharmaceutical fields. Additionally, these constituents hold significant values in the perfume, agrochemical, and cosmetic industries (Yi, Cao, Cao, & Xiao, 2019). The functional characteristics of PM are significant due to its diverse range of bioactive compounds, commonly known as secondary metabolites or phytochemicals. A study has demonstrated that PM is abundant in over 70 phytochemicals, including terpenes (monoterpenes and sesquiterpenes), aliphatic compounds, and organic acids (Ahmad et al., 2014). Moreover, to facilitate further research on the single compounds in PM, we summarized the main phytochemicals present in PM as well as their respective activities and/or applications, which are listed in Table 1.

2.2. Factors affecting the phytochemical compositions of PM

The phytochemicals or secondary metabolites of PM are commonly produced to respond to external stimuli including infection, nutrition, or alteration of climatic conditions. These phytochemicals are abundantly found in leaves, stems, and roots, but different compounds are synthesized in specific parts of the PM. Because of this, the phytochemical compositions of PM in different locations and environments are different. The factors affecting the phytochemical compositions of PM are summarized in Fig. 3.

The phytochemical compositions of PM may vary depending on the geographical location, climatic conditions, and varietal differences (Ma, Chai, Hou, Zhao, & Meng, 2022; Punia Bangar, Dunno, Kumar, Mostafa, & Maqsood, 2022; Sabaragamuwa, Perera, & Fedrizzi, 2018; Wong, Li, Li, Razmovski-Naumovski, & Chan, 2011). Notably, PM leaves from Genting Highland in Pahang, Ulu Yam in Selangor, and the lab (a controlled environment lab culturing the cuttings of PM from Genting Highland in Pahang. At 22/16 °C day/night temperatures under 12 h light/dark photoperiod with light intensity of 170 ± 20 μmol m^{-2} s^{-1} at ~75% RH.) contain different compounds, with a total of 48, 39, and 44 compounds, respectively (Baharum, Bunawan, Ghani, Wan, & Noor, 2010; Rahnamaie-Tajadod, Goh, & Mohd Noor, 2019; Rusdi et al., 2016).

Meanwhile, studies showed that the variation in composition profiles of plant materials is influenced by various factors, including the specific plant part utilized, such as barks, leaves, root barks, or buds (Graf & Stappen, 2022; Ribeiro-Santos et al., 2017). Despite the same extraction and identification methods applied to examine the constituents in PM leaves, stems, and roots from the same plant, distinct phytochemicals were obtained (Ahmad, Bunawan, Normah, & Baharum, 2016). In other words, PM leaves, stems, and roots from the same plant contain different compounds. In addition, the extraction techniques also affects the phytochemical composition (Cheng et al., 2023). Ahmad et al. (2014) used Solid Phase Microextraction (SPME) and hydrodistillation coupled with GC-MS to identify the volatile compounds present in the leaves,

Fig. 1. Appearance of *Polygonum minus* (PM). (A) Plant morphology of PM; (B) Whole plant view of PM; (C) Leaves of PM; (D) Stem of PM.

stems, and roots. Specifically, about 300 mg of fresh PM was ground with liquid nitrogen and placed in a 20 mL vial. Then 700 μL of distilled water was added to the ground leaves and the vial was covered tightly using a hole cap with septum to ensure no volatile could escape during the extraction. The fiber was then exposed to the sample headspace by inserting the fiber through the septum and the vial with the exposed fiber was incubated in a water bath at 45 °C for 15 min. After 15 min, the fiber was thermally desorbed by inserting the fiber into the GC injector at 250 °C for 10 min. On the other hand, essential oil was isolated by the hydrodistillation technique. PM (300 g) were subjected to hydrodistillation with 2 L of distilled water for 8 h using a Clevenger-type apparatus to produce a yellowish essential oil. The essential oils were collected over water, separated, dried over nitrogen gas, and stored. As a result, even though the same plant and the same part were used, different compounds were obtained due to the use of SPME or hydrodistillation respectively, as summarized in Fig. 4.

Besides, the compositions, nutritional values, and functional attributes of phytochemicals are influenced by postharvest interventions, encompassing processing (analytical methods), preservation practices, and storage methodologies (Alwazeer et al., 2023; S. Bakir et al., 2023; Cano-Lamadrid, Martínez-Zamora, Castillejo, & Artés-Hernández, 2022; Cautela, Vella, & Laratta, 2019; Dhami & Mishra, 2015; Fratianni et al., 2017; Hassan Sakar et al., 2021; Sęczyk, Ahmet Ozdemir, & Kołodziej, 2022). Markom, Hassim, Anuar, and Baharum (2012) found that 70% methanol yielded the highest total extract (33.1%) compared to other co-solvents (water, methanol, ethanol, 50% methanol, 50% ethanol, and 70% ethanol), and exhibited the highest levels of total phenolic content (TPC), total flavonoid content (TFC), ferric-reducing antioxidant power (FRAP), and 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical inhibition. Hassim, Markom, Anuar, and Baharum (2014) corroborated these findings. Conversely, Kartikasari, Rahman, Puspasari, and Ridha (2022) reported that the 50% ethanol extract of PM leaves exhibited the highest TPC, while the methanol extract showed the highest TFC. Moreover, Hassim et al. (2015) observed the ethanol co-solvent system successfully extracted all three aldehydes (decanal, dodecanal, and undecanal). Shevchenko, Muzychkina, Ross, and Korul'kin (2019) concluded that the optimal extraction of the polyphenolic phytocomplex from PM plant raw materials was achieved through repetitive extraction using 50% ethanol or 50% acetone as solvents at their boiling point. In another study, Syaiful, Jayuska, and Harlia (2015) utilized steam distillation techniques to investigate the impact of time variations on the compounds present in PM leaves. Following that, Azhari, Markom, Ismail, and Anuar (2022) utilized supercritical fluid extraction with carbon dioxide to examine the impact of CO_2 flow rates (2 mL/min, 3 mL/min, and 4 mL/min) on essential oil yield and β-caryophyllene yields from PM roots, as summarized in Fig. 5.

Overall, different processing methods led to variations in the major constituents of the plant extract, and the yield of each principal component was dependent on the specific extraction techniques employed (Ullah, Wilfred, & Shaharun, 2019). Moreover, the type and conditions of the drying treatments influenced the retention of phytochemicals. The findings of Mahanom, Azizah, and Dzulkifly (1999) indicated the herbal preparation produced through oven drying exhibited lower levels of phytochemical content compared to that obtained through freeze-drying. Azhari, Markom, Ismail, and Anuar (2020) also had similar views. Their findings revealed that an increase in drying temperature reduced essential oil yield and resulted in the loss of major chemical compounds in PM roots, and air-drying emerged as the most effective for preserving crucial chemical compounds in PM roots, including β-caryophyllene (1.43%), pentadecane (4.34%), hexadecanoic acid (3.91%), and oleic acid (3.97%). Nonetheless, all types and conditions of drying treatments were able to retain significant amounts of phytochemicals, especially carotenoids, ascorbic acid, niacin, and riboflavin (Mahanom et al., 1999).

In conclusion, the diversity observed in the composition profiles, quantities of individual components, and overall yield of oil or extract from plant materials stems from various factors. These factors encompass the choice of solvent during extraction, the physical characteristics of the sample, the plant species, the specific plant part utilized (such as barks, leaves, root barks, or buds), geographical origin, preservation methods, and encompassing processing (utilized extraction techniques and analytical methods) (Ribeiro-Santos et al., 2017).

3. Toxicity

The main concern in the toxicity of herbal remedies is their capacity to produce lethality and antagonistic impacts when consumed (Azad, Sulaiman, & Kundu, 2022). The prominent uniqueness of herbal plants is the presence of secondary metabolites as a natural defense toward plant growth. They can offer significant benefits but can also be harmful when consumed excessively (van Wyk & Prinsloo, 2020). Therefore, the valuation of toxicity is urgent and vital for medicinal plants to be used in

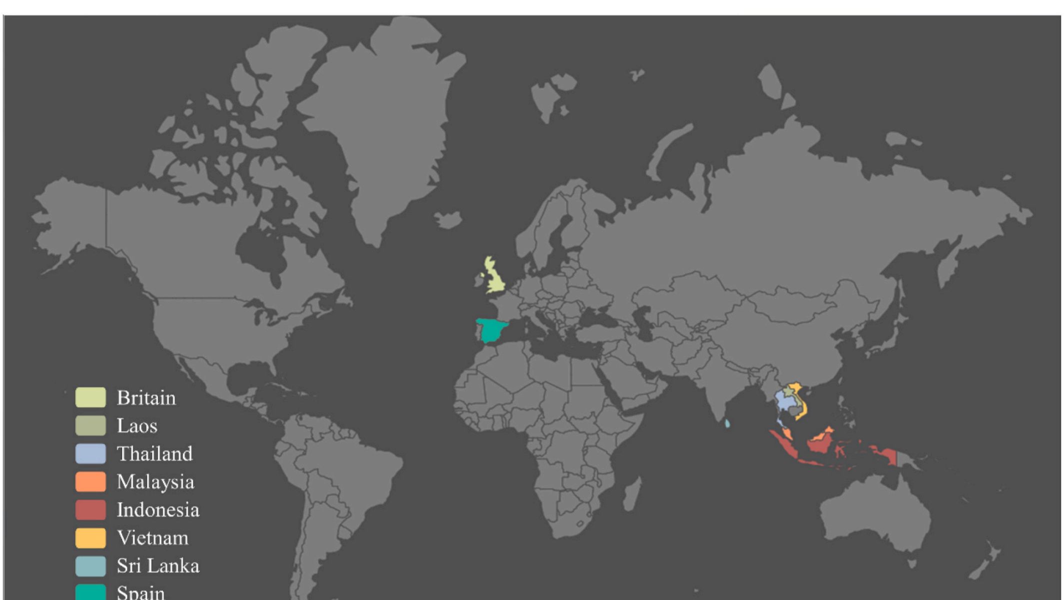

Fig. 2. Main distributions of PM in the world.

Table 1
Phytochemical compositions of PM with their activities and/or applications.

No.	Phytochemical classes	Composition	Chemical formula	Activities/Applications	Reference
1	Terpenes (Monoterpenes)	α-Pinene	$C_{10}H_{16}$	Anti-microbial; Anti-oxidant; Anti-inflammatory; Chondroprotective	(A. C. R. Da Silva et al., 2012; Rufino et al., 2014)
2		α-Thujene	$C_{10}H_{16}$	Anti-inflammatory; Anti-oxidant; Anti-microbial	Kazemi (2014)
3		Limonene	$C_{10}H_{16}$	Anti-Anxiety; Pest Control; Cosmetic; Skincare Formulations; Anti-oxidant; Insect repellent	(Ciriminna, Lomeli Rodriguez, Demma Carà, Lopez Sanchez, & Pagliaro, 2014; Hollingsworth, 2005; Song et al., 2021)
4		β-Ocimene	$C_{10}H_{16}$	Anti-fungal	Cavaleiro et al. (2015)
5		Myrtenal	$C_{10}H_{14}O$	Bronchodilatory; Anti-inflammatory; Anti-aggregative; Anti-hemolytic (*in vitro*); Anti-bacterial; Anti-tumor; Anti-hyperglycemic, Vasodilating; Heart rate reducing; Hypotensive; Anxiolytic; Anti-oxidant; Neuromodulatory; Sedative; Anti-diabetic; Analgesic; Neuroprotective	(Dragomanova, Tancheva, & Georgieva, 2018, 2019; Henriques et al., 2023)
6		-(Z)-Myrtanol	$C_{10}H_{18}O$	Sedative	De Sousa, Raphael, Brocksom, and Brocksom (2007)
7		Borneol	$C_{10}H_{18}O$	Analgesia; Putridity elimination; Flesh regeneration; Cell Protection; Anti-thrombotic	(Li, Sun, Zhang, & Wang, 2008; Xiong, Xiao, Xu, Wu, & Jiang, 2013)
8		(E)-Geranyl acetone	$C_{13}H_{22}O$	Anti-bacterial; Anti-fungal	Bonikowski, Świtakowska, and Kula (2015)
9	Terpenes (sesquiterpenes)	Germacrene D	$C_{15}H_{24}$	Mosquito repellency; Anti-aphid; Anti-tick	(J. Liu et al., 2022)
10		Isocaryophyllene	$C_{15}H_{24}$	Anti-fungi; Anti-cancer	(Legault & Pichette, 2010; Sabulal et al., 2006)
11		Copaene	$C_{15}H_{24}$	Anti-oxidant; Cytotoxic; Anti-genotoxic	Türkez, Çelik, and Toğar (2014)
12		α-Zingiberene	$C_{15}H_{24}$	Anticancer; Treatment of chronic wounds; Anti-inflammatory; Angiogenesis suppressing	(Ferreira et al., 2022; Seshadri et al., 2022)
13		δ-Elemene	$C_{15}H_{24}$	Anti-cancer; Anti-oxidant; Reversal of Drug Resistance	Tan et al. (2021)
14		Aromadendrene	$C_{15}H_{24}$	Anti-fungal; Anti-bacterial; Anti-viral; Plant growth regulatory; Anti-feedant; Repellent; Cytotoxic; Spasmolytic	(Asakawa, Yoyota, Takemoto, Kubo, & Nakanishi, 1980; Capon & MacLeod, 1988; Gaspar-Marques, Simões, & Rodríguez, 2004; Harada, Sakata, & Ina, 1984; Hubert, Okunade, & Wiemer, 1987; Matsuo, Atsumi, Nakayama, & Hayashi, 1981; Messer et al., 1990; Moreira, Lago, Young, & Roque, 2003; Murata et al., 1990; Pérez-Hernández, Ponce-Monter, Ortiz, Cariño-Cortés, & Joseph-Nathan, 2009; Su et al., 2008; Tada & Yasuda, 1985; Tommasi, Pizza, Conti, Orsi, & Stein, 1990)
15		(E)-α-Bergamotene	$C_{15}H_{24}$	Insecticidal; Anti-diabetic; Anti-inflammatory; Anti-microbial; Anti-oxidant; Anti-cancer	(Ahmed et al., 2019; Annaz et al., 2023; Bayala et al., 2014; Magalhães et al., 2010; Niu et al., 2021; Urzúa et al., 2010; Ying et al., 2017)
16		β-Guaiene	$C_{15}H_{24}$	Anti-inflammatory	Sahi (2016)
17		4,11-selinadiene	$C_{15}H_{24}$	Not reported	\
18		β-Caryophyllene	$C_{15}H_{24}$	Anti-inflammatory, Anti-diabetic, Anti-tumor, Neuroprotective; Anti-oxidant; Anti-convulsant; Analgesic; Myorelaxant; Sedative; Anti-depressive; Treatment Streptococcus infections, osteoporosis, and steatohepatitis	(Bahi et al., 2014; B. Bakir, Him, Özbek, Düz, & Tütüncü, 2008; Basha & Sankaranarayanan, 2014; Dahham et al., 2015; de Oliveira et al., 2018; Francomano et al., 2019; Legault & Pichette, 2010; Machado et al., 2020)
19		Eremophilene	$C_{15}H_{24}$	Insecticidal; Anti-bacterial	(Deng et al., 2022; Utegenova et al., 2018)
20		β-farnesene	$C_{15}H_{24}$	Insecticidal	Sun et al. (2011)
21		Sesquiphellandrene	$C_{15}H_{24}$	Anti-viral	(Denver, Jackson, Loakes, Ellis, & Young, 1994; Joshi, Sunil Krishnan, & Kaushik, 2020; Zhuang et al., 2012)
22		Alloaromadendrene	$C_{15}H_{24}$	Anti-oxidant	(Abd-ElGawad, Elshamy, El-Nasser El Gendy, Al-Rowaily, & Assaeed, 2019; Abd-Elgawad et al., 2021)
23		α-Bisabolene	$C_{15}H_{24}$	Anti-inflammatory; Food flavoring; Anti-cancer	(Jou et al., 2016; C. Wang, Zada, Wei, & Kim, 2017; Y. Zhao et al., 2021)
24		α-Panasinsen	$C_{15}H_{24}$	Not reported	\
25		α-Cedrene	$C_{15}H_{24}$	Anti-obesity; Trypanocidal; Anti-leukemic	(T. H. Kim et al., 2015; Nibret & Wink, 2010)
26		Valencene	$C_{15}H_{24}$	Anti-allergic; Anti-melanogenesis; Anti-septic; Anti-oxidant; Synergistic anti-colon cancer effect with doxorubicin	(Ambrož et al., 2015, 2017; Gallily, Yekhtin, & Hanuš, 2018; Jin, Lee, Kim, & Kim, 2011; K. Liu, Chen, Liu, Zhou, & Wang, 2012; Tsoyi et al., 2011; I. J. Yang, Lee, & Shin, 2016)
27		Nerolidol	$C_{15}H_{26}O$	Anti-oxidant; Anti-microbial; Anti-inflammatory; Anti-nociceptive; Anti-parasitic; Anti-ulcer; Skin penetration Enhancement; Insect repellent; Anti-cancer; Anti-biofilm; Insecticidal; Anti-tumor; Anti-nociceptive	(Biazi, Zanetti, Baranoski, Corveloni, & Mantovani, 2017; Chan, Tan, Chan, Lee, & Goh, 2016; Goel, Kaur, & Pahwa, 2016; Javed, Azimullah, Abul Khair et al., 2016; Lee et al., 2007; Nogueira Neto et al., 2013; Russo, 2011; Saito et al., 2016; Tatman & Mo, 2002)
28		α-Himachalene	$C_{15}H_{24}$	Against coronavirus and HIV-1; Anti-cancer; Anti-inflammatory	(Ajlaoui et al., 2024; Chaudhary et al., 2014; Elias et al., 2019; Faris et al., 2023)
29		Cadinene	$C_{15}H_{24}$	Anti-oxidant	Kundu, Saha, Walia, Ahluwalia, and Kaur (2013)

(*continued on next page*)

Table 1 (*continued*)

No.	Phytochemical classes	Composition	Chemical formula	Activities/Applications	Reference
30		Gurjunene	$C_{15}H_{24}$	Anti-oxidant; Anti-bacterial	Namata Abba, Ilagouma, Amadou, and Romane (2021)
31		Caryophyllene oxide	$C_{15}H_{24}O$	Anti-fungal; Anti-inflammatory; Analgesic; Anti-cancer; Insecticidal; Anti-feedant; Anti-platelet aggregation; Preservative in food, drugs, and cosmetics	(Bettarini et al., 1993; Fidyt, Fiedorowicz, Strządała, & Szumny, 2016; Gyrdymova & Rubtsova, 2022; Javed, Azimullah, Haque, & Ojha, 2016; Langenheim, 1994; Lin et al., 2003; Russo, 2011; Sain et al., 2014; D. Yang, Michel, Chaumont, & Millet-Clerc, 2000)
32		Humulene epoxide	$C_{15}H_{24}O$	Anti-oxidant	(P. Sharma & Shah, 2015)
33		Seychellene	$C_{15}H_{24}$	Anti-inflammatory	(Luo et al., 2019; L. Zhang et al., 2021)
34		α-Curcumene	$C_{15}H_{22}$	Anti-Tumor; Anti-breast cancer	(Al-Amin, Rahiman, Khairuddean, & Salhimi, 2023; Y. Shin & Lee, 2013)
35		Cubenol	$C_{15}H_{26}O$	Anti-bacterial; Anti-oxidant; Anti-microbial; Anti-fungal; Insecticidal	(Basile et al., 2022; Bueno, Escobar, Martínez, Leal, & Stashenko, 2011; Djeddi et al., 2012; González et al., 2012; Mancini, De Martino, Malova, & De Feo, 2013; Moiteiro et al., 2013; Takao et al., 2012)
36		Thujopsene	$C_{15}H_{24}$	Anti-fungal	Syahmina and Usuki (2020)
37		Longipinocarvone	$C_{15}H_{22}O$	Not reported	\
38		Aristolene	$C_{15}H_{24}$	Not reported	\
39		dehydro- Cyclolongifolene oxide	$C_{15}H_{22}O$	Anti-oxidant	Abd-ElGawad et al. (2023)
40		α-Cadinol	$C_{15}H_{26}O$	Anti-mite; Anti-bacterial; Anti-fungal; Anti-oxidant	(Chang, Chen, Wang, & Wu, 2001; González et al., 2012)
41		β-Bisobolol	$C_{15}H_{26}O$	Not reported	\
42		α-Eudesmol	$C_{15}H_{26}O$	Anti-microbial; Anti-tumor	(Britto et al., 2012; Ho, Wang, Hsu, Lee, & Su, 2009)
43		Drimenol	$C_{15}H_{26}O$	Anti-feedant; Anti-bacterial; Anti-fungal; Cytotoxic; Insecticidal; Anti-allergic; Piscicidal; Molluscicidal; Regulating the plant growth	(T. de M. Silva et al., 2013; Vlad, 2006)
44		Isolongifolol	$C_{15}H_{26}O$	Not reported	\
45		Drimenin	$C_{15}H_{22}O_2$	Anti-fungal; Anti-bacterial; Anti-fungal; Anti-feedant; Plant-growth regulatory; Cytotoxic; Phytotoxic; Piscicidal; Molluscicidal	(Jansen & De Groot, 2004; Paz et al., 2020)
46	Aliphatic compounds	Undecane	$C_{11}H_{24}$	Anti-inflammatory; Anti-allergic	(D. Choi, Kang, & Park, 2020)
47		Decanal	$C_{10}H_{20}O$	Anti-oxidant; Flavor and fragrance applications; Inhibitory and bactericidal; Cytotoxic	(K. Liu et al., 2012)
48		Decane, 4-methyl	$C_{11}H_{24}$	Not reported	\
49		Decanol	$C_{10}H_{22}O$	Not reported	\
50		Undecanal	$C_{11}H_{22}O$	Anti-bacterial	(Basu & Banik, 2020; Faudale, Viladomat, Bastida, Poli, & Codina, 2008)
51		Cyclohexane, 1-ethenyl-1-methyl-2,4-bis(1-methylethene)	$C_{15}H_{24}$	Not reported	\
52		Dodecanal	$C_{12}H_{24}O$	Anti-microbial	Chanprapai, Kubo, and Chavasiri (2018)
53		Pentadecane	$C_{15}H_{32}$	Anti-microbial; Cytotoxic; Anti-parasitic	Bruno et al. (2015)
54		1-Dodecanol	$C_{12}H_{26}O$	Anti- fungal; Anti-microbial	Chanprapai et al. (2018)
55		Pentadecanal	$C_{15}H_{30}O$	Anti- biofilm	Casillo et al. (2017)
56		Heptadecane	$C_{17}H_{36}$	Anti-inflammatory; Anti-proliferative; Anti-aging	(D. H. Kim et al., 2013; L. C. Wu, Ho, Shieh, & Lu, 2005)
57		Octadecane	$C_{18}H_{38}$	Not reported	\
58		1-Hexadecanol	$C_{16}H_{34}$	Not reported	\
59		Eicosane	$C_{20}H_{42}$	Anti-fungal	Ahsan, Chen, Zhao, Irfan, and Wu (2017)
60		Tetracosane	$C_{24}H_{50}$	Not reported	\
61		Bicyclo[5.3.0]decane, 2-methylene-5-(1-methylvinyl)-8-methyl-	$C_{15}H_{24}$	Anti-microbial; Anti-inflammatory; Anti-oxidant; Anti-proliferative; Anti-cancer; Anti-tumors; Anaesthetic	(Shaheena, Chintagunta, Dirisala, & Sampath Kumar, 2019; Zahin, Ahmad, & Aqil, 2017)
62		Bicyclo[5.2.0]nonane, 2-methylene-4,8,8-trimethyl-4-vinyl-	$C_{15}H_{24}$	Not reported	\
63		Naphthalene, 1,2,3,4,4a,5,6,8a-octahydro-4a,8-dimethyl-2-(1-methylethenyl)-,	$C_{15}H_{24}$	Anti-inflammatory; Anti-microbial; Anti-cancer	(M. H. Huang et al., 2003; Ibrahim & Mohamed, 2016; Osmaniye et al., 2023)
64		Phytane	$C_{20}H_{42}$	Not reported	\
65		Perhydrofarnesyl acetone	$C_{18}H_{30}O$	Not reported	\
66		3,7,11,15-Tetramethyl-2-hexadecen-1-ol	$C_{20}H_{40}O$	Fragrance ingredient	McGinty, Letizia, and Api (2010)
67		Phytol	$C_{20}H_{40}O$	Anxiolytic; Metabolism-modulating; Cytotoxic; Anti-oxidant; Autophagy and apoptosis inducing; Anti-nociceptive; Anti-inflammatory; Anti-microbial; Immune-modulating; Anti-tumor; Anti-mutagenic; Anti-atherogenic; Anti-diabetic; Lipid-lowering; Anti-spasmodic; Anti-epileptic; Anti-nociceptive; Anti-depressant	(Alencar et al., 2018; Islam et al., 2018)

(*continued on next page*)

Table 1 (*continued*)

No.	Phytochemical classes	Composition	Chemical formula	Activities/Applications	Reference
68	Organic acids	Dodecanoic acid	$C_{12}H_{24}O_2$	Anti-bacterial; Anti-oxidant; Anti-apoptotic	Renugadevi, Valli Nachiyar, and Zaveri (2021)
69		Myristoleic acid	$C_{14}H_{26}O_2$	Cytotoxic	Iguchi et al. (2001)
70		Tetradecanoic acid	$C_{14}H_{28}O_2$	Anti-microbial	(Bharathy, Sumathy, & Uthayakumari, 2012; Mujeeb, Bajpai, & Pathak, 2014)
71		Pentadecanoic acid	$C_{15}H_{30}O_2$	Anti-bacterial; Anti-fungal; Anti-inflammatory; Anti-fibrotic; Red blood cell stabilizing; Mitochondrial repairing; Essential fatty acid; Regulation of stemness in breast cancer cells; Anti-proliferative; Cytotoxic; Anti-cancer; Anti-microbial	(To, Nguyen, Moon, Ediriweera, & Cho, 2020; S. Venn-Watson, Lumpkin, & Dennis, 2020; S. K. Venn-Watson & Butterworth, 2022)
72		Hexadecanoic acid	$C_{16}H_{32}O_2$	Anti-cancer; Anti-inflammatory; Anti-bacterial; Anti-oxidant; Anti-microbial	(Aparna et al., 2012; Shaaban, Ghaly, & Fahmi, 2021; Sianipar, Purnamaningsih, & Rosaria, 2016; Siswadi & Saragih, 2021)
73		Oleic acid	$C_{18}H_{34}O_2$	Anti-fungi; Immunomodulatory; Blood pressure reducing; Regulating body weight	(Alonso-Torre, Carrillo, & Cavia, 2012; Owolabi, L, & B, 2018; Terés et al., 2008; Tutunchi, Ostadrahimi, & Saghafi-Asl, 2020)
74		Octadecanoic acid	$C_{18}H_{36}O_2$	Anti-oxidants; Anti-microbial; Anti-inflammatory; Anti-cancer; Anti-measles virus	(Entigu, Linton, Lihan, & Ahmad, 2013; Mujeeb et al., 2014; Othman, Abdullah, Ahmad, Ismail, & Zakaria, 2015; Reza et al., 2021; Siswadi & Saragih, 2021)
75		Hexanedoic acid	$C_6H_{10}O_4$	Anti-bacterial; Anti-microbial	(W. H. Choi & Jiang, 2014; Iornumbe, Yiase, & Ato, 2016; Sianipar et al., 2016; Siswadi & Saragih, 2021)
76		2-Propenoic acid	$C_3H_4O_2$	Not reported	\
77		1,2-Benzenedicarboxylic acid	$C_8H_6O_4$	Cytotoxicity; Anti-microbial; Anti-cancer; Anti-bacterial	(Albratty et al., 2021; Krishnan, Mani, & Jasmine, 2014; Shoge, Garba, & Labaran, 2017)

Table 2
PM-induced toxic effects.

Category	Plant part	Solvent used in plant solvent extraction	Model	Highest dose	Results	Reference
Acute toxicity	Leaf	Water	Rats	5 g/kg bw	Non-toxic	(S. Q. Wasman et al., 2010)
	Stem and leaf	Water		2000 mg/kg bw		Ming et al. (2013)
	Leaf	Water		2000 mg/kg bw		(N. Muhammad et al., 2013)
	Leaf	Methanol		2000 mg/kg bw		(P. V. Christapher et al., 2017)
Sub-acute toxicity	Stem and leaf	Water	Rats	1000 mg/kg bw	Non-toxic	Ming et al. (2013)
	Leaf	Water	Rats	2000 mg/kg bw	Large dose whereby it may lead to electrolyte imbalance, anemia, and hypocalcemia	(N. Muhammad et al., 2013)
	Leaf	Methanol	Rats	2000 mg/kg bw	Non-toxic	(P. V. Christapher et al., 2017)
Genotoxicity	Leaf	Water	Human lymphocytes	\	No genotoxic	Wan-Ibrahim, Sidik, and Kuppusamy (2010)
	Stem and leaf	Methanol	Zebrafish		No teratogenic	Omar, Kue, Dianita, and Yu (2020)

medicine and pharmacology (Pham et al., 2023). Table 2 and 3 summarize the toxicity of PM in detail, including acute toxicity, subacute toxicity, genotoxicity, and cytotoxicity.

3.1. Acute toxicity

An acute toxicity study examines potential harmful effects that arise when organisms are exposed to single or multiple doses of a test substance within 24 h through various routes like oral, dermal, or inhalation (Saganuwan, 2017). The information gathered from the acute toxicity study serves as a guide for determining appropriate dosage levels in long-term toxicity studies and other animal research (Erhirhie, Ihekwereme, & Ilodigwe, 2018).

PM has well-established traditional applications in folk medicine and, in general, is believed to be safe. Even so, it is essential to experiment with its safety level for long-term usage. The acute toxicity assessment of PM aqueous leaf extract appears promising, as no adverse effects were observed in experimental animals during a 14-day observation period. It is reported that, in the acute toxicity test, oral administration of 2000 mg/kg of the PM aqueous extract produced neither mortality nor changes in behavior or any other physiological activities (Ming, Zulkawi, Cy, & Choudhary, 2013; N. Muhammad et al., 2013). The highest administered dose of 5 g/kg body weight (bw) did not induce any toxicity, as examination of the liver and kidney in treated rats revealed no significant changes compared to the control group. Hematology and clinical biochemistry values fell within the range of those observed in control animals. This indicates that the PM aqueous leaf extract is relatively non-toxic (S. Q. Wasman, Mahmood, Salehhuddin, Zahra, & Salmah, 2010). Another study found that the methanol extract of PM at 2000 mg/kg did not exhibit any signs of acute toxicity. Thus, the LD_{50} is determined to be greater than 2000 mg/kg (P. V. Christapher et al., 2017). According to Sharma et al. (2020), all the test animals stayed healthy and exhibited normal behavior throughout the experiment, so this herb could be considered safe. Therefore, PM could be considered a tool for developing medications to address contemporary health issues.

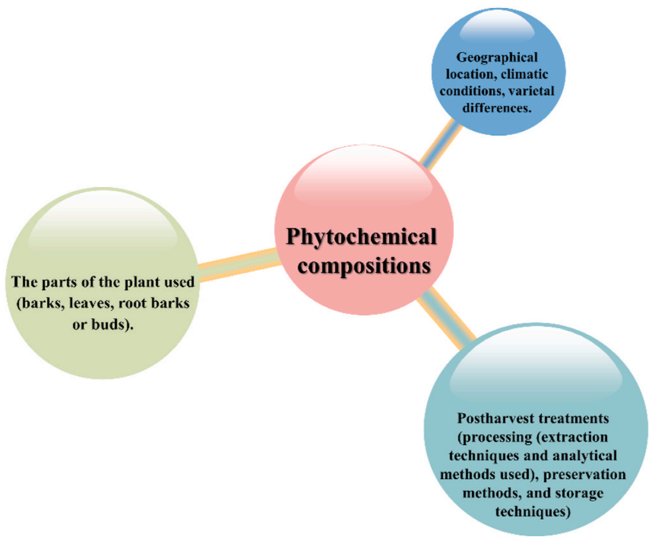

Fig. 3. Factors affecting the phytochemical compositions of PM.

3.2. Sub-acute toxicity

The sub-acute toxicity study is essential for the assessment of the safety of an agent when it is administered repeatedly over a period of time (P. V. Christapher et al., 2017) because subacute toxicity determines the long-term adverse effects of the repeated daily dose administration (Nakakaawa, Gbala, Cheseto, Bargul, & Wesonga, 2023).

In a subacute 28-day repeated dose oral toxicity study, no mortality or toxic signs were observed when the three doses of 125, 500, and 1000 mg/kg of PM aqueous extract were administered orally for a period of 28 days (Ming et al., 2013). In the subacute toxicity study led by Muhammad and colleagues, the results indicated an absence of toxicity, behavioral changes, or fatalities during the study. However, when the extract was given at a dose of 2000 mg/kg bw for 14 days, there was a significant reduction in hemoglobin, calcium, and sodium levels, along with an increase in potassium levels. In summary, oral administration of PM leaf extract did not induce subacute toxicity in male rats, except at an extremely high dose, which could lead to electrolyte imbalance, anemia, and hypocalcemia (N. Muhammad et al., 2013). The study by Christapher et al. revealed that the methanol extract of PM leaves does not possess any neurotoxicity as the animals were normal. The locomotor activity of the treated group of animals was compared and found no reduction or stimulation. Thus, the result indicates the absence of any inhibitory or stimulatory activity on the mental activity. In the present study, chronic treatment of PM methanol extracts up to 2000 mg/kg did not produce any mortality (P. V. Christapher et al., 2017).

Thus far, sub-chronic and chronic toxicological studies have not been carried out on various parts and solvent extracts of PM. Hence, a thorough toxicological evaluation of the safety level of the extracts is required for consideration of PM as an innocuous herbal drug.

3.3. Genotoxicity

Studies have revealed that some plants frequently used in folk medicine are potentially genotoxic (Ananthi, Chandra, Santhiya, & Ramesh, 2010; Marques, De Medeiros, Da Silva Dias, Barbosa-Filho, & Agnez-Lima, 2003; Melo-Reis, Bezerra, Vale, Canhête, & Chen-Chen, 2011; Regner et al., 2011; I. S. Shin et al., 2011). Wan-Ibrahim et al. have proved that aqueous extract of PM has no genotoxic effect on human lymphocytes (Wan-Ibrahim et al., 2010). Omar and colleagues investigated the teratogenic potential of PM using a zebrafish model. The results showed that the tested methanol extract of PM did not interfere with the development of zebrafish embryogenesis (Omar et al., 2020).

3.4. Cytotoxicity

Over the past decade, a number of *in vitro* methods have been evaluated with the aim of replacing the mouse bioassay for toxicity testing. Cell culture-based toxicity tests are of interest, having the potential to detect more general cytotoxicity endpoints (Dzoyem, Kuete, McGaw, & Eloff, 2014).

For cancer cells, the PM leaf 50%, 70%, and 100% ethanol extracts showed significant suppression of viability of HCT116, HT29, and CT26 cell lines (Rohin et al., 2020), and meanwhile PM leaf 100% ethanol extract showed antiproliferative activity on HeLa cells (Ali et al., 1996; Rohin et al., 2020). However, PM leaf acetone extract displayed no toxicity against the HCT116, HT29, and CT26 cell lines (Rohin et al., 2020). This indicates that the function of the extracts can be influenced by the choice of various extraction solvents. In addition, the ethyl acetate extract of PM leaf had potent cytotoxicity against HCT116, HT29, CT26, HeLa, and HepG2 cell lines (Abdullah et al., 2017; Mohd Ghazali

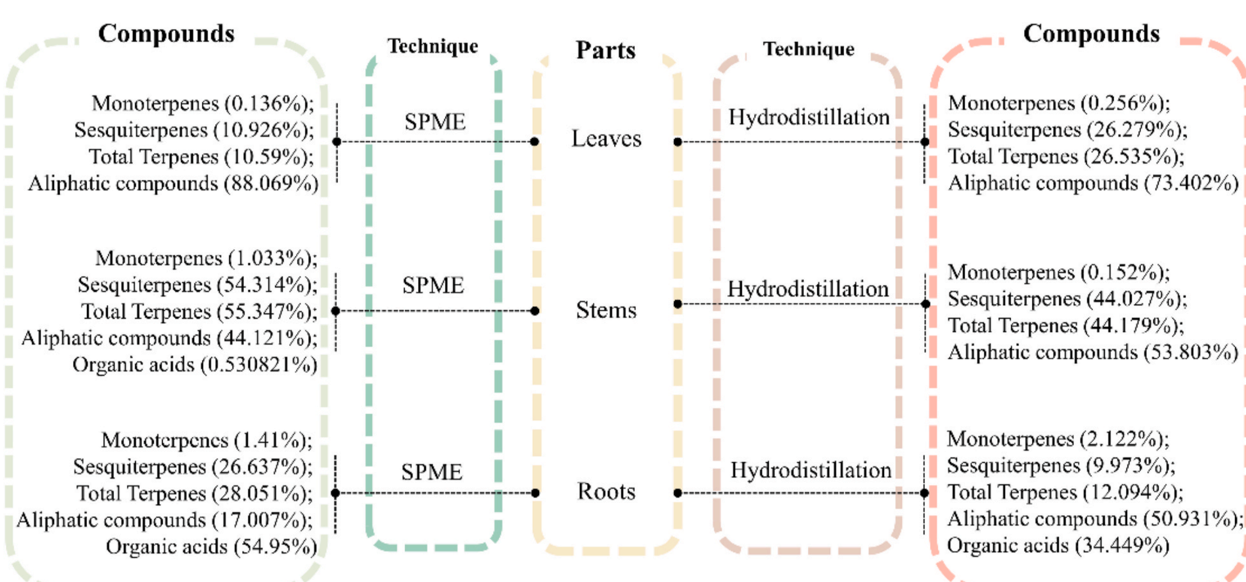

Fig. 4. Plant parts and extraction techniques affect phytochemical composition.

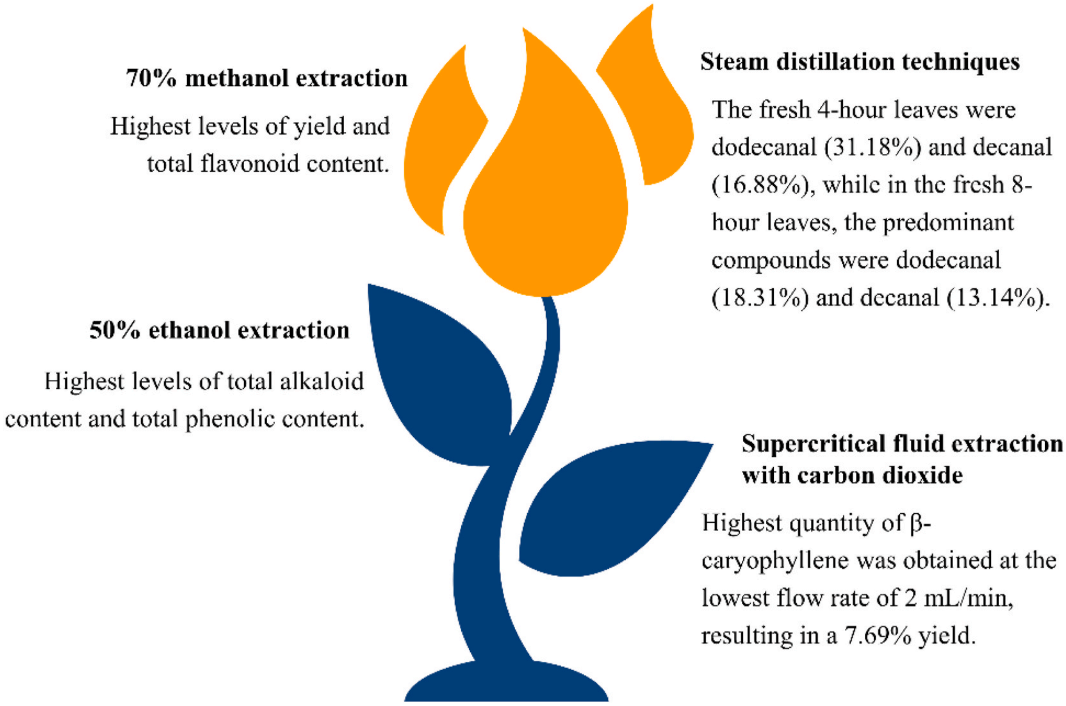

Fig. 5. Extraction affects the phytochemical composition.

et al., 2014; Rohin et al., 2020). The PM leaf ethyl acetate extract showed cytotoxicity toward MCF7 cells, but $IC_{50} > 250$ μg/mL (Mohd Ghazali et al., 2014). The hexane extract of PM leaf exhibited promising cytotoxicity against the HCT116 cells with an IC_{50} value of 40 μg/mL (Abdullah et al., 2017). Another study showed that PM leaf methanol extract had antiproliferative effects against HCT116, HT29, CT26, and HeLa cell lines, and cytotoxicity toward HepG2 and MCF7 cells, but $IC_{50} > 250$ μg/mL (P. V. Christapher, Parasuraman, et al., 2016; Mohd Ghazali et al., 2014; Rohin et al., 2020). Research findings showed that petroleum ether extract from PM leaf was able to suppress the growth of HCT116, HeLa, HepG2, and MCF7 cells (Mohd Ghazali et al., 2014). Besides, another *in vitro* experiment showed that water extract of PM possessed antiproliferative effects against a panel of cancer cells, including HCT116, HT29, CT26, HeLa, HepG2, and MCF7 cells (P. V. Christapher, Parasuraman, et al., 2016; Mohd Ghazali et al., 2014; Rohin et al., 2020).

For normal cells, the water, ethanol, ethyl acetate, methanol, and petroleum ether extracts of PM leaf showed no activity against the Hs888Lu and Vero cells and gave an $IC_{50} > 250$ μg/mL for CCD841, Chang liver, and WRL-68 cells (Abdullah et al., 2017; Mohd Ghazali et al., 2014; Qader et al., 2011; Vimala et al., 2011; Wahab et al., 2015). In addition, on the CCD841 and EA.hy926 cells, PM leaf hexane, methanol, and water extracts demonstrated cytotoxic action, while on the Vero cell, PM stems methanol extract demonstrated cytotoxic action (Abdullah et al., 2017; P. V. Christapher, Parasuraman, et al., 2016; Wahab et al., 2015).

Consequently, some PM extracts have been verified to treat cancers effectively due to their lower toxicity and minimal side effects on normal cells. This high selectivity makes it a safe option for managing and treating cancer.

According to Table 3 and it is evident that researchers using the same solvent extract obtained varying results on identical cells. Some demonstrated robust cytotoxic activity effects, while others exhibited weaker ones. This variability may be attributed to differences in the plant phytochemical compositions, influenced by geographical location, climate, and variations in plant varieties (as summarized in part 2).

4. Traditional usages

The whole parts of this plant (aerial, root, root bark, stem, stem bark, flower, and seeds) are used for various purposes (P. V. Christapher et al., 2017). PM is traditionally used as a food and flavoring agent (Abdullah et al., 2017; Han et al., 2024). In Japan, China, and Europe, PM has long been applied as a hot-tasting spice (Ahmad et al., 2014). In Malaysia, PM is frequently added to vegetable salad and many other dishes as a flavoring enhancer (Abdullah et al., 2017), such as laksa (spicy noodle dish), kerabu (fried herbal rice), asam pedas (spicy tamarind curry), and tom yam (spicy tangy soup) (Rahim et al., 2022; Vimala, Adenan, Ahmad, & Shahdan, 2003). The Malaysian Government has listed this plant in the National Agro-Food Policy to ensure sufficient food supply (Embong, 2007). In Indonesia, particularly in West Kalimantan, padas porridge made using PM is commonly known as the unique cuisine of West Kalimantan (Alves, Ribeiro, Kloos, & Zani, 2001; Phatik, Das, & Boruah, 2014). Moreover, PM is also an important traditional medicine for relieving physical discomforts, including rid of fungal infections, treating poor eyesight, and alleviating body aches as well as others.

Given various biological activities besides enhancing the flavor of food dishes (Imelda et al., 2014), traditionally, PM leaves are used as medicine for the treatment of different ailments (Hassan, Noor, & Kader, 2015, pp. 41–48). It has been used to treat digestive disorders (George, Ng, O'Callaghan, Jensen, & Wong, 2014; Han et al., 2024), reduce dandruff (Z. Muhammad & Mustafa, 2015), treat poor eyesight (Jarukamjorn & Nemoto, 2008), warm the body up (Embong, 2007), improve blood circulation (Vikram et al., 2014), get rid of fungal infections (Ong & Nordiana, 1999), alleviate body aches (Amiruddin, Wahab, & Mohsin, 2020; Wiart, 2006)), and be a beverage after childbirth (P. Christapher, Vikneswaran, et al., 2015). In India, PM has been applied as diuretics, central nervous system stimulants, diaphoretics, and styptics (Ahmad et al., 2016). Moreover, most Chinese Buddhists have taken the leaves primarily for the fact that PM can reduce sexual desire; thus, the monks usually grow PM as their garden plant and consume it as a supportive stride in their celibate life (Abubakar et al., 2015). Fig. 6 displays the traditional application of PM in ethnopharmacology.

Table 3
Detailed information on cytotoxicity of PM.

Plant part	Solvent used in plant solvent extraction	Cells	IC$_{50}$	Reference
Leaf	Ethanol	HeLa	0.1 mg/mL	Ali et al. (1996)
Leaf	Water Ethanol	Hs888Lu	No cytotoxicity	Qader et al. (2011)
Leaf	Water	WRL-68 Vero	No cytotoxicity	Vimala et al. (2011)
Leaf	Petroleum ether	HepG2	>250 μg/mL	Mohd Ghazali et al. (2014)
		WRL-68	56.23 μg/mL	
		HeLa	127.21 μg/mL	
		HCT116	145.32 μg/mL	
		MCF7	>250 μg/mL	
		Chang liver	>250 μg/mL	
	Methanol	HepG2	>250 μg/mL	
		WRL-68	>250 μg/mL	
		HeLa	205 μg/mL	
		HCT116	86.3 μg/mL	
		MCF7	>250 μg/mL	
		Chang liver	>250 μg/mL	
	Ethyl acetate	HepG2	32.25 μg/mL	
		WRL-68	122.38 μg/mL	
		HeLa	63.09 μg/mL	
		HCT116	199.52 μg/mL	
		MCF7	>250 μg/mL	
		Chang liver	285.72 μg/mL	
	Water	HepG2	>250 μg/mL	
		WRL-68	>250 μg/mL	
		HeLa	>250 μg/mL	
		HCT116	>250 μg/mL	
		MCF7	>250 μg/mL	
		Chang liver	>250 μg/mL	
Leaf	Methanol	Vero	875 mg/L	Wahab, Bunawan, and Ibrahim (2015)
Stem			95 mg/L	
Leaf	Water	HCT116	>200 μg/mL	(P. V. Christapher, Parasuraman, et al., 2016)
		HT29	>200 μg/mL	
		HeLa	>200 μg/mL	
		EA.hy926	92.2 μg/mL	
Leaf	Methanol	HCT116	>200 μg/mL	
		HT29	>200 μg/mL	
		HeLa	>200 μg/mL	
		EA.hy926	214 μg/mL	
Leaf	Hexane	HCT116	40 μg/mL	Abdullah, Mohd Ali, Abolmaesoomi, Abdul-Rahman, and Hashim (2017)
		CCD841	190.62 μg/mL	
	Ethyl acetate	HCT116	43.18 μg/mL	
		CCD841	89.2 μg/mL	
	Methanol	HCT116	>333 μg/mL	
		CCD841	>333 μg/mL	
	Water	HCT116	>333 μg/mL	
		CCD841	>333 μg/mL	
Leaf	Water	HT29	75 μg/mL	Rohin, Hadi, and Ridzwan (2020)
		HCT116	33 μg/mL	
		CT26	29 μg/mL	
	Methanol	HT29	78 μg/mL	
		HCT116	30 μg/mL	
		CT26	20 μg/mL	
	Ethanol	HT29	73 μg/mL	
		HCT116	31 μg/mL	
		CT26	26 μg/mL	
	70% Ethanol	HT29	34 μg/mL	
		HCT116	13 μg/mL	
		CT26	10 μg/mL	
	50% Ethanol	HT29	24 μg/mL	
		HCT116	20 μg/mL	
		CT26	23 μg/mL	
	Acetone	HT29 HCT116 CT26	No cytotoxicity	
	Ethyl acetate	HT29	33 μg/mL	
		HCT116	7 μg/mL	
		CT26	7 μg/mL	

5. Food application

Recent studies found that PM had different applications in the food field such as food formulation and encapsulation. Therefore, PM and their bioactive properties hold significant potential for utilization in diverse food industry contexts as illustrated in Fig. 7.

5.1. Food additive

In recent decades, particular attention has been emphasis on the importance of natural products in safeguarding meat products against spoilage (Konfo et al., 2023). Antioxidants, functioning as hydrogen atom donors, are utilized in meat products to retard or prevent oxidative reactions (Hadidi et al., 2022). The incorporation of plant extracts as food additives serves to diminish the reliance on synthetic additives while addressing the demand for natural food options (Santos et al., 2022). This situation also poses a new challenge for food scientists who are actively seeking novel natural sources of antioxidant molecules for potential use as food additives (Felipe Alzate-Arbeláez, Dorta, López-Alarcón, Cortés, & Rojano, 2019). On the other hand, to ensure the microbial safety of food products, the food industry employs various preservatives (Premanath, James, Karunasagar, Vaňková, & Scholtz, 2022). Natural plant extracts are recognized as effective natural antimicrobial agents and thus gaining importance as food additives (Friedlein, Dorn-In, & Schwaiger, 2021; N. Sharma & Gulati, 2023).

PM exhibits antioxidant attributes, as evidenced by spent hen meat burgers containing PM water extracts, which displayed significantly lower peroxide value (PV) and thiobarbituric acid (TBA) values in comparison to the control group over a three-month frozen (−18 °C) storage period (Huda-Fujan, Noriham, Norrakiah, & Babji, 2006). Similarly, in a separate study, the PM extract-treated duck meatballs demonstrated superior antioxidant effects, texture, and microbial potency compared to the control group Abdul Azziz et al. (2015)during

Table 4
Summary of the inhibition effects of PM on the bacterium.

Plant part	Extraction method	Solvent used	Method	Inhibited bacterium	Reference
Leaf	Solvent extraction	n-Hexane	Disk diffusion method	*Staphylococcus aureus, Staphylococcus epidermidis, and Streptococcus pyogenes*	(P.M. Ridzuan et al., 2013)
		Dichloromethane		*Staphylococcus aureus, Staphylococcus epidermidis, and Streptococcus pyogenes*	
		Methanol		*Staphylococcus aureus and Staphylococcus epidermidis*	
		Water		*Staphylococcus aureus and Streptococcus pyogenes*	
Leaf	The first stage covers extraction, which was done by steam distillation to obtain essential oils, followed by multilevel extraction by maceration and UAE to obtain different extracts	Ethanol	Disc diffusion method	*Staphylococcus aureus*	Imelda, Kusumaningrum, and Faridah (2013)
Leaf	Ultrasound-assisted extraction	Ethanol	Macro dilution method	*Staphylococcus aureus*	Imelda et al. (2014)
Leaf	Solvent extraction	Water	Agar well diffusion	*Staphylococcus aureus, Staphylococcus epidermidis,*	Hassan et al. (2015)
		Methanol		*Staphylococcus aureus and Staphylococcus epidermidis,*	
		Ethanol		*Staphylococcus aureus and Staphylococcus epidermidis*	
Leaf	Solvent extraction	30% Water -ethanol and 100% Water	Disc diffusion and microplate dilution	*Staphylococcus aureus*	Abubakar et al. (2015)
Leaf	Solvent extraction	Methanol	Disc diffusion method	*Staphylococcus aureus*	Zamri (2015)
Leaf and the whole plant	Soxhlet extraction	Methanol and distilled water extracts	Disc diffusion method	*Staphylococcus aureus*	Hassim et al. (2015)

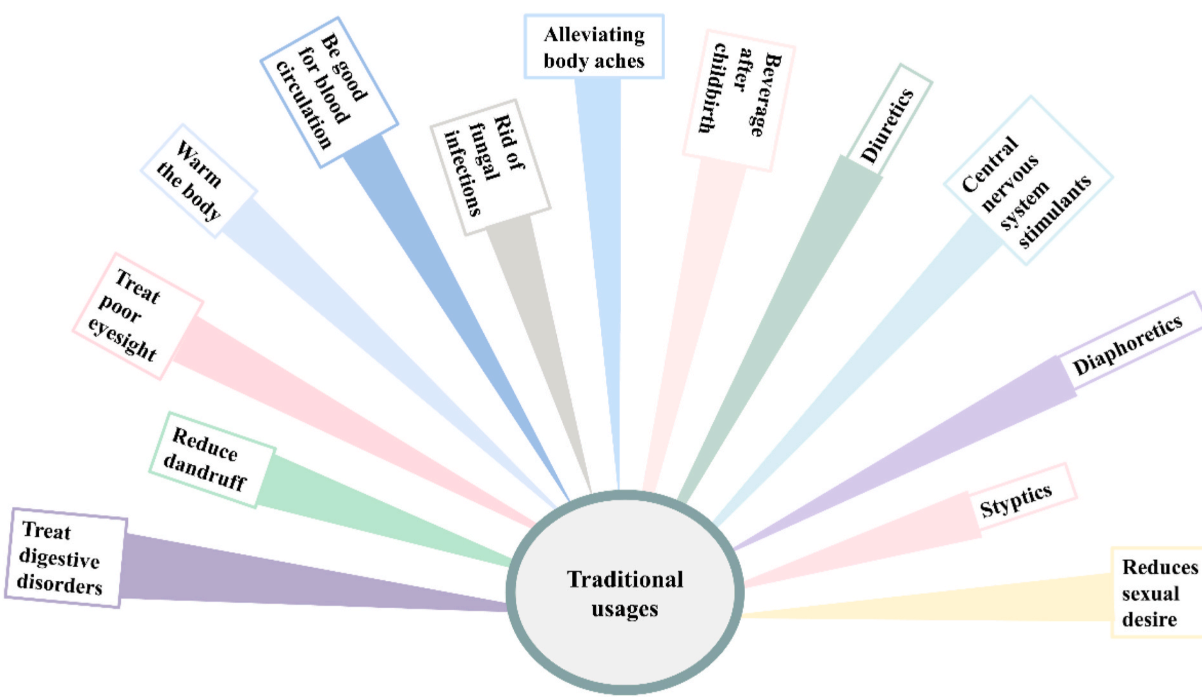

Fig. 6. Traditional medicine uses of PM.

refrigerated storage (±4 °C) over 21 days (Nurul, Ruzita, & Aronal, 2010). In addition, after 21 days of storage, quail meatballs formulated with PM extract exhibited lower TBA, free fatty acid (FFA), PV values, and aerobic plate count compared to the control (Ikhlas, Huda, & Ismail, 2012). Overall, the above study suggests PM extracts have the potential to serve as a natural antioxidant resource for extending the shelf life of meatballs, and resembling the synthetic antioxidant hydroxy anisole (BHT) (Ikhlas et al., 2012; Nurul et al., 2010). Moreover, since Ikhlas et al. (2012) discovered that PM extract decreased FFA levels in food products, where FFA is known to affect the color and taste of a food leading to reduced consumer acceptance (Sete da Cruz et al., 2022), thus Gervacia and Ratih (2021) investigated the addition of PM leaves to waste cooking oil to reduce FFA content. The results were gratifying, with an average reduction in FFA levels of 7.12% in used cooking oil

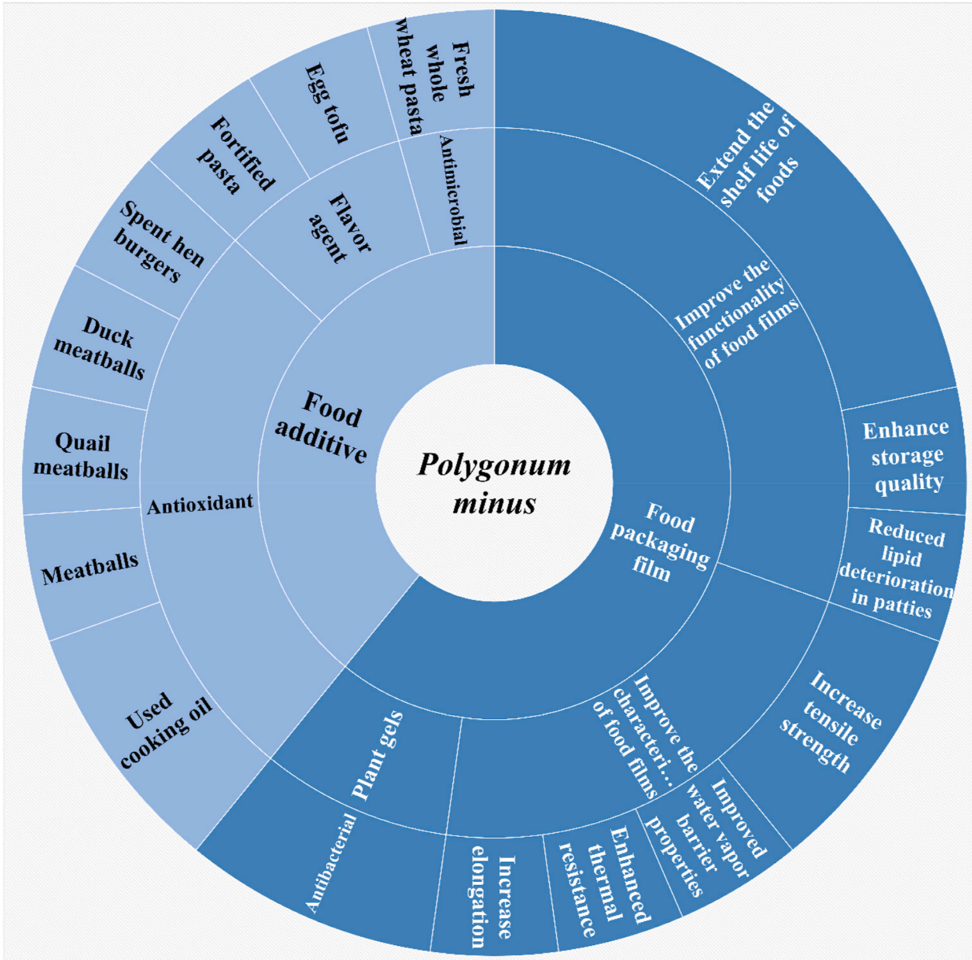

Fig. 7. Application of PM in food products and food packaging film.

before adding PM leaves. A positive correlation was established between the addition of PM leaves and the reduction in fatty acid levels (Gervacia & Ratih, 2021). In essence, achieving lower FFA content in oils by using the antioxidant properties of PM leaves is desirable for enhancing their quality (Mataruco et al., 2023).

PM demonstrates potent antimicrobial properties, as highlighted in a study by Abdul Azziz et al. (2015), wherein the hexane extract of PM exhibited remarkable efficacy against various food bacteria in the disk diffusion method. Afterward, researchers considered whether incorporating PM as an antibacterial agent would impact consumer acceptance of food products. To assess this, they added dry PM powder to fresh whole wheat pasta and stored it under refrigeration (4 °C) and at ambient temperature (24 °C). Notably, the study found that whole wheat pasta supplemented with PM powder showed comparable overall acceptance to control pasta, with no significant differences (Az-Zahra Tashim, Harkani, Abdullah Lim, & Maryam Basri, 2021). This suggests the potential for plant powder additions to serve as potent bio-preservatives and antimicrobial agents without compromising consumer acceptance (Az-Zahra Tashim et al., 2021).

To assess the impact of incorporating PM into food on consumer sensory perception, researchers experimented with adding PM to egg tofu. The results revealed that an increase in PM content significantly enhanced the springiness of the egg tofu, with the optimal formula combination of 0.7% PM, 0.5% *Curcuma longa*, and 0.8% *Zingiber officinale* (Maizura, Aminah, & Wan Aida, 2016). In another investigation, Tashim, Lim, and Basri (2022) observed that adding PM powder to pasta resulted in favorable sensory acceptability. The fortified pasta, enriched with the PM powder mixture significantly increased DPPH scavenging activity while retaining characteristics indistinguishable from the control pasta, including minimal cooking loss and favorable cohesiveness, springiness, and chewiness (Tashim et al., 2022).

In short, PM holds promising prospects as a food additive. On one hand, its antioxidative properties can effectively delay or prevent the oxidation reaction of food. On the other hand, its antibacterial attributes can prevent food from being contaminated by microbes. Moreover, incorporating PM into food can enhance sensory acceptance among consumers.

5.2. Food packaging film

Food packaging primarily aims to shield food from contaminants and extend its shelf life (Kola & Carvalho, 2023). However, the global food industry has a significant environmental impact, primarily due to the extensive use of petroleum-based plastic packaging films (Babayev et al., 2023; R. Westlake et al., 2023; W. Zhang, Roy, Ezati, Yang, & Rhim, 2023). Considering environmental concerns, there is a growing focus on replacing synthetic polymers with renewable, biodegradable films. These biodegradable films offer advantages including biocompatibility, edibility, non-toxicity, and a wide range of potential applications. This shift towards biodegradable films is regarded as an innovative and effective alternative for extending the shelf life of various food products (Manzoor, Yousuf, Ahmad Pandith, & Ahmad, 2023; Díaz-Montes & Castro-Muñoz, 2021; Kaya et al., 2018; Suvarna, Nair, Mallya, Khan, & Omri, 2022).

PM extracts have been found to improve the characteristics of food films. Yahaya, Husaini, Zaharudin, and Azman (2020) reported that adding 2% PM extract to semi-refined carrageenan plasticized with glycerol can increase tensile strength and elongation at break values to improve film properties. In other words, adding PM extract to a semi-refined carrageenan-based film can make the film durable and strong (Yahaya et al., 2020). Other researchers had similar reports, and they found that PM at a 10% weight percentage was incorporated into polylactic acid (PLA) to create PLA-10PM packaging films using the solvent-casting method. PLA-10PM demonstrated enhanced thermal resistance and improved water vapor barrier properties (Mohamad et al., 2020). Another study found that adding PM leaf extract increased the tensile strength of edible films made from durian seed starch-chitosan, but also resulted in a decrease in film uniformity and changes in the surface appearance of the film (Lestari, Hartanti, & Permadi, 2020). In a later study, Kong, Heng, and Pui (2022) also found that PM leaf extract and curry leaf extract (CLE) were added to chitosan-based films. With the increase of PM leaf extract and CLE, the mechanical strength of the chitosan film decreased and the water solubility increased. Moreover, the addition of PM and CLE resulted in a darker, greener, less yellow color compared to regular films. Hence, adding PM leaf extract into chitosan-based films remains a challenge, and we still need to optimize the preparation method of this film. Furthermore, polybutylene succinate (PBS) film containing PM displayed a cohesive structure according to morphological analysis (Mohamad et al., 2022).

PM extracts have also been found to improve the functionality of food films. Husna Abd Hamid and the team successfully developed a semi-refined carrageenan film containing α-tocopherol and PM extract that can extend the shelf life of foods with high-fat content (Husna Abd Hamid et al., 2019). Subsequently, Yahaya and the team found that a semi-refined carrageenan film containing 2% PM extract significantly reduced lipid deterioration in patties and reduced metmyoglobin value changes (Yahaya, Almajano, Yazid, & Azman, 2019). As reported, PLA-10PM could preserve chicken meat for up to 15 days while maintaining odorless and firm textural properties (Mohamad et al., 2020). Kong et al. (2022) also had similar research results. Chicken breast meat wrapped with chitosan films containing 2.0% (w/v) PM and 2.0% (w/v) CLE remained viable at 4 °C for 14 days. The film extended the shelf life of chicken breasts by at least 2 days (Kong et al., 2022). In a study by Lestari, Hartanti, and Permadi (2020), the findings indicated that using an edible coating made of durian-chitosan seed starch with PM leaf extract could prolong the shelf life of beef sausage by four months when stored at freezing temperatures (Lestari, Permadi, & Mulyadi, 2022). The quality of chicken fillets coated with active PBS films improved in terms of color attributes when loaded with 15% PM (Mohamad et al., 2022). In addition to meat, edible films containing PM extracts can enhance the lipid oxidation stability and storage quality of apples (Husaini & Azman, 2020). Therefore, active packaging of edible films incorporating PM extracts shows potential as food packaging applications to extend the shelf life of meat, fruits, and vegetables (Husaini & Azman, 2020; Mohamad et al., 2020).

Moreover, in food packaging, in addition to food films, there are also coatings applied around the surface of the food (Mohamed, El-Sakhawy, & El-Sakhawy, 2020). Plant gels have an important role in food preservation as edible coatings (Kahramanoğlu, Chen, Chen, & Wan, 2019) and are generally applied by dipping the foods, spraying, or brushing. To date, numerous studies have been conducted on the use of PM gel as an edible coating. Pramita investigated the antibacterial properties of methanol extract from PM leaves and its effectiveness when formulated into a gel product. Gel C (15% methanol extract) exhibited the most potent antimicrobial effect, suggesting its potential as an antiseptic agent. Furthermore, Gel C demonstrated better stability in all variables of the gel stability test compared to Gel A (5% methanol extract) and Gel B (10% methanol extract) (Pramita, 2013). Another study had a similar view. Gel C experienced the least viscosity decrease, while Gel B showed the least reduction in thickening ability, an increase in pH, and improved spreadability (Ansiah, 2014).

In summary, PM extract shows great use and bright prospects in the food industry. On the one hand, it can be added to food as a food additive, and on the other hand, it can also be used as an edible film and gel to protect food from contaminants. An in-depth investigation of the vital components within PM extracts is necessary before processing them further for use in food formulation and packaging.

6. Agricultural field

Given the frequent occurrence of disease in the livestock breeding and aquaculture industry, the use of chemicals and antibiotics is increasingly restricted by governments, as well as the low feed conversion ratio. Thus, herbal feed additives have become a focus of research and development. This section reviewed some studies on the application of PM in livestock poultry breeding and aquaculture industry, as shown in Fig. 8.

6.1. Livestock and poultry

Poultry and livestock products are valuable sources of proteins and minerals (Abd El-Hack et al., 2022). However, the industry faces various environmental challenges like slow growth of animals, and hazards of parasites causing significant economic losses globally (El-Shall et al., 2022; Salem et al., 2022). Currently, there is a global initiative to explore natural drug alternatives to enhance poultry and livestock production while avoiding the residual impact associated with drug use in these products (Rehman et al., 2020).

PM usage as an anti-parasite has also raised substantial concern in animal husbandry. The results of the study by Alawiyah, Kahtan, and Widiyantoro (2016) showed that there was no significant difference in the death time of *Ascaris gallinae* between the PM extract concentration of 2 mg/mL and the albendazole group, indicating that the methanol extract of PM leaves has comparable anthelmintic activity to albendazole. The study found no significant difference in the time of death for the worms between the PM leaves ethanol extract concentration of 2 mg/mL and treated with Albendazole at 0.2 mg/mL. This indicates that the 2 mg/mL concentration of the ethanol extract from PM leaves exhibits comparable anthelmintic activity to Albendazole at 0.2 mg/mL (Maulidya, Kahtan, Natalia, Handini, & Vidiyantoro, 2018). In addition to chicken parasites, PM extract can also inhibit the growth of sheep parasites. *Haemonchus contortus* is a nematode commonly found in sheep, causing issues like hemorrhagic anemia or even death (Flay, Hill, & Muguiro, 2022). A previous study evaluated the effectiveness of ethanolic PM extracts in inhibiting egg hatch and larval development assays of *H. contortus*. Results showed that PM extract exhibited larvicidal properties against *H. contortus*, indicating its potential to hinder parasite development (N. N. H. Yahya, 2017).

Additionally, PM can be used as a feed additive to improve chicken production. Basit et al. (2020) found that adding PM leaf meal to the diet improved growth performance, blood parameters, and serum biochemistry in broiler chickens. Remarkably, there were no harmful effects observed in the liver histomorphology. This suggests that PM leaf meal of feed can be safely used as an alternative to traditional growth promoters for broiler chickens. Another study investigated PM as a feed additive in the diet of *Kampung Unggul Balitbangtan* chickens to enhance their overall performance. It has been demonstrated that adding 2% PM powder during the starter period significantly improved the feed gain ratio in these chickens (Febriyanto, Lestari, & Tribudi, 2021).

In short, PM extract can inhibit the growth of parasites and has a significant anthelmintic effect on some parasites (its anthelmintic activity is equivalent to albendazole). PM leaf powder feed can promote the growth of broiler chickens without toxic side effects. Given that PM feed has anti-parasitic qualities, it can be utilized safely as an alternative to conventional growth promoters in broiler farms.

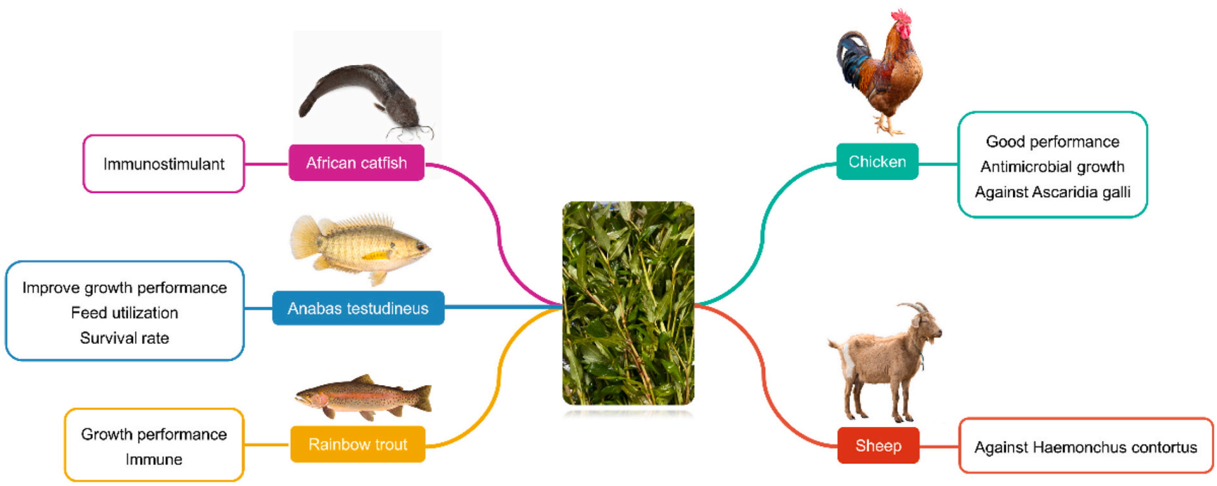

Fig. 8. Application of PM in the breeding industry.

6.2. Aquatic products

The aquaculture industry is a vital source of nutritious and affordable protein, particularly through fish and shrimp farming (Abdel-Latif et al., 2022). Across the globe, farmers are increasingly turning to intensive culture systems to meet the rising demand for these seafood products. However, the high fish biomass in confined spaces of intensive systems often leads to disease outbreaks (Abdel-Latif, Dawood, Menanteau-Ledouble, & El-Matbouli, 2020, 2022; Abdel-Latif & Khafaga, 2020; El-Son, Nofal, & Abdel-Latif, 2021). To address this, researchers have explored various feed supplements for farmed fish, including herbal extracts and essential oils, to promote immune function, support microbiota, improve growth, and prevent diseases (Awad & Awaad, 2017; Bulfon, Volpatti, & Galeotti, 2015; Citarasu, 2010; Galina, Yin, Ardó, & Jeney, 2009; Harikrishnan, Balasundaram, & Heo, 2011; Newaj-Fyzul & Austin, 2015; Reverter, Bontemps, Lecchini, Banaigs, & Sasal, 2014; Van Hai, 2015).

Veerasamy et al. (2014) investigated the impact of the aqueous extract of PM leaves on the hematological parameters and lysozyme activity in *Clarias gariepinus*. The findings suggest that the extract could serve as an immunostimulant for African catfish, but careful monitoring may be necessary for prolonged use. Similarly, Panase and Tipdacho (2018) conducted a study on *Anabas testudineus* fingerlings, applying PM leaf extract at different levels for 60 days. Their results indicated improved growth performance, especially in feed utilization, and increased survival rates during the fingerling nursing phase. Moreover, the use of herbal extracts positively affected white blood cell counts. Adel, Dawood, Shafiei, Sakhaie, and Shekarabi (2020) explored the effects of PM extracts on rainbow trout, focusing on growth, skin mucus, serum immune parameters, and immune-related gene expressions. Rainbow trout-fed diets with varying PM levels (0, 5, 10, and 15 mg/kg) for 8 weeks exhibited significant improvements in final bw, weight gain, and specific growth rate. Therefore, the above studies confirm the positive effects of dietary PM on fish growth and immunity.

7. Medicinal field

Medicinal plants, recognized for their chemical compositions (Hayat et al., 2022), hold crucial pharmaceutical and therapeutic values (Begum, Hamayun, Tabassum Yaseen, Sumbal Akhter, & Muhammad, 2016). They have historically been utilized across cultures (Khumalo, Van Wyk, Feng, & Cock, 2022) and continue to serve as fundamental resources for enhancing human health (Bernardini, Tiezzi, Laghezza Masci, & Ovidi, 2017). Additionally, they contribute significantly to the development of modern medicines, nutraceuticals, food supplements, and pharmaceutical products (Dias, Urban, & Roessner, 2012). In developing nations, about 80% of the population is dependent on traditional medicines which are reported to be a combination of phytochemical and herbal plants for curing various diseases (Chilvery et al., 2023). PM is a plant that contains several bioactive compounds with potential medicinal properties which are useful in fighting and treating common ailments, as well as inhibiting effects on microbes (Ahmad et al., 2018, 2023; P. V. Christapher, Parasuraman, et al., 2015; Qader et al., 2011; Vikram et al., 2014). The protective effects of PM in body systems are summarized in Fig. 9, and each study is discussed in the following sections.

7.1. Integumentary system

The skin acts as a critical interface between the body and the external environment, serving as a primary barrier against environmental factors and pathogens (Grice, 2014). Its main function is to protect the body from microorganisms, toxins, and various external factors, thus preventing potential harm and maintaining overall health (Goceri, 2019; Grice & Segre, 2011; Larouche, Sheoran, Maruyama, & Martino, 2018; Rousselle, Braye, & Dayan, 2019). Nevertheless, skin infections are a common reason for consultations in primary health care centers, and the most common bacteria causing skin infections (CBSIs) are *Staphylococcus aureus, Staphylococcus epidermidis, and Streptococcus pyogenes* (Mussin et al., 2021; Severn & Horswill, 2023). Fortunately, according to studies in recent years, a large number of PM extracts have shown anti-CBSIs activity. Table 4 summarizes the antibacterial activity of different solvent extracts of PM from previous studies. Besides, as summarized in part 2 (Phytochemical), PM functional attributes are influenced by postharvest interventions, encompassing processing (utilized extraction techniques and analytical methods), preservation practices, and storage methodologies. Therefore, we suggest that it is necessary to conduct in-depth studies on the anti-CBSIs activity of PM hexane extracts.

It is well known that fungi form a commensal relationship with human skin (Hurabielle et al., 2020). However, when the immune system is compromised, fungi can become opportunistic pathogens, evading the host immune system and leading to frequent and severe infections (Köhler, Casadevall, & Perfect, 2015). The findings of Dewi and her team revealed that the ethanol extract exhibited antifungal activity against *Trichophyton rubrum* (Dewi, Asseggaf, Natalia, & Mahyarudin, 2019). Melinda and her team measured the inhibition zone diameters and found that the ethanol extract exhibited antifungal activity against *Trichophyton mentagrophytes* at concentrations of 40% and 80%, with average inhibition zone diameters of 10.125 mm and 20.625

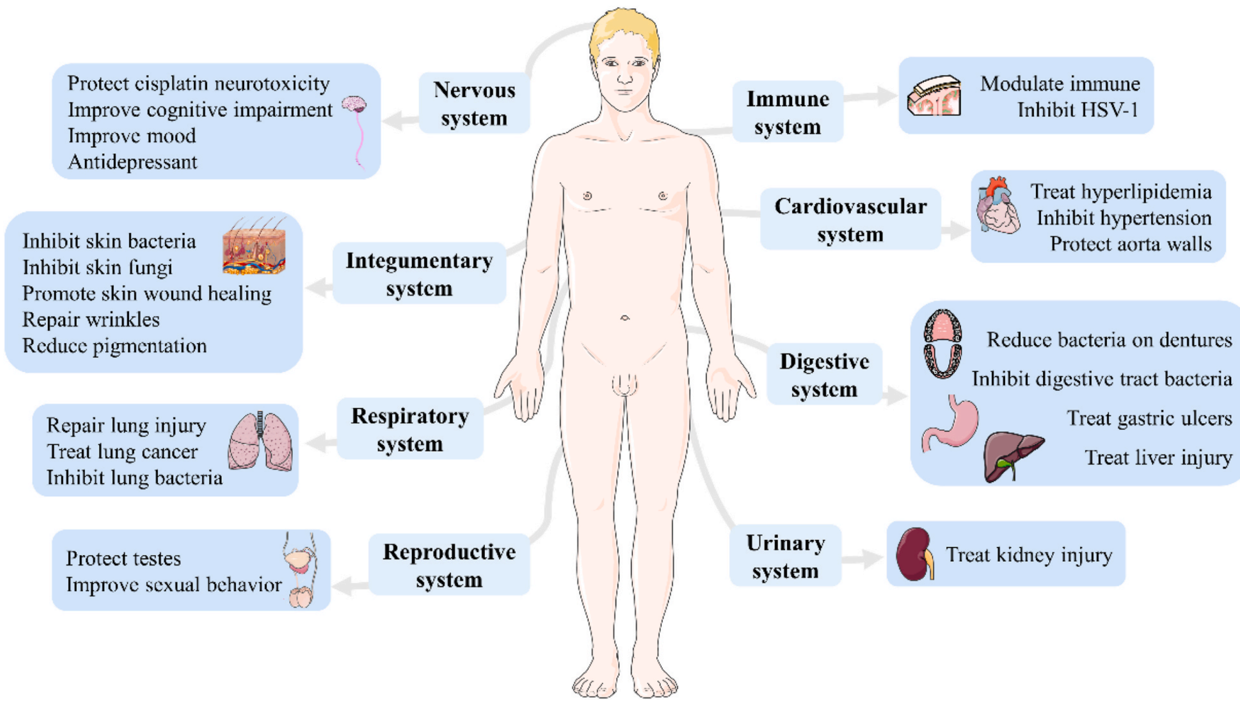

Fig. 9. Protective effects of PM in body systems.

mm, respectively (Melinda, Asseggaf, Mahyarudin, & Natalia, 2019). Moreover, the ethanol extract did not create an inhibitory zone on the growth of *Microsporum gypseum*, indicating a lack of antifungal activity against this fungus (Liauw, Asseggaf, & Natalia, 2021). Dandruff causes itchy, flaking skin with mild inflammatory reactions and is also one of the most common and widely seen dermatological diseases that affect the majority of the world population (Sheth & Dande, 2021). PM leaves were divided into four shampoo formulas by varying concentrations of PM leaves ethanol extract: 0%, 5 %, 10 %, and 15 %. The shampoo formula of PM leaves ethanol extract showed that it had antifungal activity against the fungi that caused dandruff. The best inhibitor activity was obtained from the third formula, with the diameter of a clear zone at 2.61 cm (Hadiarti, 2017).

Skin damage has become a clinical problem, that not only affects the body and mind of patients but also causes great loss to society (Liang et al., 2021). It acts as the initial defense barrier against microbes, preventing their unrestricted access to internal organs and potentially fatal consequences (Goceri, 2019; Larouche et al., 2018; Rousselle et al., 2019). Elnehrawy (2015) conducted a study to assess the effectiveness of various PM leaf extracts in promoting wound healing. Aqueous (31 μg/mL) and ethanol extract (63 μg/mL) of PM leaves significantly enhanced cellular migration and wound closure by 71% and 65% on day 1, respectively. The induced scratch was fully healed on day 2 with aqueous and ethanol extracts. Consequently, the aqueous extract of PM leaves may contribute to enhancing the healing capacity of skin cells, offering a safer, more natural, and cost-effective remedy. Hypersensitivity to mosquito bites is characterized by intense local skin responses to mosquito bites and various systemic symptoms (Vander Does, Labib, & Yosipovitch, 2022). In local reactions, mosquito bites can cause clear or hemorrhagic blisters of the skin, accompanied by intense red swelling (Hirai et al., 2023). These reactions can progress to necrosis or ulcers, ultimately healing with lasting scarring on the skin (Tatsuno et al., 2016). Some studies demonstrated that the methanol extract from PM had repellent and knockdown effects on *Musca domestica*. The 10% concentration of the extract showed the highest repellent effect at 61.67%, falling into the moderate category. Additionally, the 25% concentration was more effective in causing knockdown, reaching 75%, with the first knockdown observed in the 40 min (Kumalasari, Rima Setyawati, & Hepi Yanti, 2015). Nugraha explored whether the n-hexane extract of PM leaf has an effect as a mosquito repellent and how it is effective when formulated in gel products with different concentrations. The results showed that the gel had a few changes in all variables of evaluation, but it was good enough esthetically for a month and could be used on the skin (Nugraha, 2021).

Beyond mere protection, skin health and appearance play crucial roles in self-esteem and social interactions (Khmaladze, Leonardi, Fabre, Messaraa, & Mavon, 2020). Beautiful, even-toned, blemish-free skin is everybody's dream (de Souza, 2008). However, no one can avoid pigmentation and wrinkles in the skin. Therefore, it is important to find bioactive substances that combat pigmentation and wrinkles. Skin hyperpigmentation is a disorder that causes blotchy, discolored, or darker skin tone in comparison with normal skin (M. C. Kang et al., 2020). Cosmeceuticals with biologically active ingredients that demonstrate both therapeutic and pharmaceutical effects are commonly used for reducing melanin content by inhibiting major regulatory steps in melanin synthesis and selectively targeting the hyperplastic melanocytes (Poulose et al., 2020; Sarkar, Arora, & Garg, 2013). In addition, cosmeceuticals with high antioxidant contents have been shown to be effective in reducing hyperpigmentation in the skin induced by UV radiation (Nahhas et al., 2019). In a particular investigation, the compounds from both PM leaves and rhizomes were extracted using hot water (100 °C), fresh water, and 80% ethanol individually. Subsequently, Yusuf discovered the potential of medicinal plant as an antioxidant, suggesting its applicability in producing herbal-based products in cosmetics and pharmaceuticals (Yusuf, 2014). It has been found that a wide variety of new cosmeceuticals and formulas can facilitate the skin to repair wrinkles, leading to a younger healthy-looking face (Mukherjee, Maity, Nema, & Sarkar, 2011). Haris, Ming, Perin, Blanche, and Jinapong (2014) conducted a study to assess the safety and effectiveness of Lineminus + PM cream compared to its placebo in healthy Asian females (split-face). The findings indicated that Lineminus + PM cream is safe exhibits anti-wrinkle effects, and possesses beneficial cosmetic properties for reducing wrinkles. Another study suggested that, along with PM-recognized antioxidant efficacy, the plant extract also demonstrated a noticeable clinical anti-wrinkle effect by reducing crow's feet wrinkles. Muthukumarasamy and colleagues concentrated on creating and assessing an herbal antioxidant cream using the methanol leaf extract of PM. The resulting antioxidant cream, derived from the methanol leaf extract of PM, demonstrated promising free radical scavenging activity. This discovery highlights the plant's significance in future research and raises its profile in the herbal and cosmetic industry (Muthukumarasamy et al., 2018).

7.2. Respiratory system

Lung diseases involve abnormalities in the lungs, stroma, and alveoli, potentially leading to fatal outcomes (Aboushanab, El-Far, Narala, Ragab, & Kovaleva, 2021). A study by Wibowo, Anwari, Aulanni'am, and Rahman (2010) revealed that the n-hexane extract reduced lung cell proliferation in animal models. Another study focused on the n-hexane fraction impact on inducing apoptosis in lung tissue epithelial cells exposed to benzopyrene. The results indicated that the n-hexane fraction not only decreased lung reactive oxygen species levels in the animal models but also induced apoptosis in the lung epithelial cells (Wibowo, Purnomo, Widodo, & Aulanni'am, 2012). Subsequently, their team compared the effects of n-hexane, ethyl acetate, and methanol fractions of PM leaf extracts in repairing lung injuries caused by benzopyrene exposure. The research, using a single dose (100 mg/kg), showed that the n-hexane fraction was the most effective in repairing lung injuries induced by benzopyrene exposure (Wibowo, Widodo, Purnomo, & A, 2013). Therefore, PM application in the adjuvant treatment of lung cancer and lung injuries merits to be considered. On the other hand, *Streptococcus pneumoniae* is the most frequent bacterial cause of community-acquired pneumonia (Suaya et al., 2021), while *Serratia marcescens* assumes an opportunistic role in respiratory infections (Luttmann, Starnes, Haddad, & Duggan, 2022). Fortunately, extracts from the PM plant exhibit inhibitory effects against these bacteria. A study by Ridzuan et al. showed that both PM leaf n-hexane and methanol extracts possess antibacterial activity against *Streptococcus pneumonia* (P.M. Ridzuan et al., 2013). Furthermore, PM leaf water, methanol, and ethanol extracts have been observed to exhibit activity against *Serratia marcescens* (Hassan et al., 2015).

7.3. Digestive system

The prevalence of oral fungal infections has significantly changed in recent years, primarily due to an increase in predisposing factors such as immune-compromising situations (e.g., HIV infection, endocrine disorders, immunosuppressive drug use, prolonged antibiotic therapies, malnourishment, and denture use) (Gleiznys, Zdanavičienė, Žilinskas, Eglė, & JuozasŽilinskas, 2015). Consequently, Rezki, Halimah, Maryani, and Setyowati (2020) explored the antibacterial effects of PM infusion extracts on bacterial colonization on acrylic dentures in the mouth. The findings indicated that PM could reduce bacterial colonies on acrylic dentures, and the antibacterial effect increased with higher infusion concentrations.

In addition, there are many bacteria that cause digestive tract diseases including *Salmonella typhi* and *Escherichia coli*, as well as leading agents of induced foodborne diseases, such as *Salmonella Typhimurium* and *Bacillus cereus* (Bernal-Bayard & Ramos-Morales, 2018; Devlin et al., 2022; Jovanovic, Ornelis, Madder, & Rajkovic, 2021; Knecht, Cholewińska, Jankowska-Mąkosa, & Czyż, 2020). However, surprisingly, PM extract was also able to inhibit these bacteria. Researchers found that PM leaf dichloromethane extract had an inhibitory effect on *Salmonella typhi* (P.M. Ridzuan et al., 2013). At the same time, PM leaf methanol extract had an inhibitory effect on *Bacillus cereus* (Zamri, 2015). Then, Imelda and his team found that PM leaf ethanol extract had inhibitory effects on *Escherichia coli* (Imelda et al., 2013). In subsequent experiments, they verified this finding (Imelda et al., 2014). This conclusion was also supported by Hassan et al. (Hassan et al., 2015). Not only that, PM leaf methanol, distilled water, and PM leaf 30% water-ethanol extracts also showed inhibitory effects on *Escherichia coli* (Abubakar et al., 2015; Hassan et al., 2015; Hassim et al., 2015). PM leaf methanol and water extracts showed inhibitory effects on *Salmonella typhimurium* (Hassan et al., 2015).

Gastric ulcer is the most common digestive tract disease (Beiranvand & Bahramikia, 2020). If not treated in time, gastric ulcers will develop into gastritis, gastric bleeding, and even gastric cancer, endangering the life of patients (Scherübl, 2020). Therefore, finding and applying natural medicines with low toxicity and good biological activity to prevent gastric ulcers has gradually become the focus of researchers (X. Wang, Wang, Wen, & Li, 2023). The findings by Wasman et al. (2010) indicated that PM exhibited anti-ulcer activity, as evidenced by reduced ulcer areas, decreased edema, and decreased leucocyte infiltration in the submucosal layer. Their separate study had similar findings, suggesting that PM could be a promising plant for the treatment of gastric ulcers (S. Wasman, Ameen, Chua, & Hamdan, 2012). Researchers have also used elution solvents to separate PM leaves into different fractions to understand the pharmacological mechanisms behind the anti-ulcer activity of PM. The findings indicated that the ethyl acetate: methanol 1:1 fraction was the most effective in providing mucous protection in the ethanol induction model. The protective mechanisms were linked to the production of antioxidants and prostaglandin E2 (Qader, Abdulla, Chua, Sirat, & Hamdan, 2012).

The worldwide occurrence of liver disease continues to be a significant concern, with liver disease being the foremost cause of illness and mortality globally, resulting in a substantial public health challenge (Asrani, Devarbhavi, Eaton, & Kamath, 2019; Byass, 2014; Xiao et al., 2019). Drug-induced liver injuries from medications, in particular, have become a growing health problem (Fu et al., 2023). A study conducted by Thanapakiam et al. (2016) revealed that both aqueous and methanolic extracts of PM have substantial hepatoprotective properties. This finding is corroborated by other scientists who suggested that incorporating PM leaves into the diet could serve as a recommended approach to counteracting various types of chemical-induced liver damage (P. V. Christapher, Joe, et al., 2016). In addition, Manoontri, Joe, Tanusha, Parasuraman, and Christapher (2016) evaluated that the higher PM dose displayed substantial hepatoprotective activity. The histopathology study further confirmed the protective effect and the efficacy increased with the dosage.

Cisplatin is a well-known platinum-based anticancer agent, which is highly effective in treating various cancers (Abd Rashid et al., 2021). Hepatotoxicity has also been demonstrated in the patients who received low doses of cisplatin, which, probably due to cumulative effect in the liver, causes massive hepatic toxicity, including dissolution of hepatic cords, focal inflammatory lesions, and necrosis (Pratibha, Sameer, Rataboli, Bhiwgade, & Dhume, 2006; Singh & Khajuria, 2015). Fajar, Kusharyanti, and Wahdaningsih (2016) revealed that cisplatin-induced hepatotoxicity, leading to elevated levels of aspartate aminotransferase (AST) and alanine aminotransferase (ALT), along with a significant degree of liver damage compared to the control group. However, the ethyl acetate fraction from PM leaves exhibited hepatoprotective activity, as evidenced by reduced levels of AST and ALT. Moreover, Rashid et al. found PM given at 100 mg/kg had preventive effects against cisplatin-induced hepatotoxicity in rats (Rashid et al., 2019). Furthermore, they discovered PM essential oil at a dose of 100 mg/kg may protect against cisplatin-induced hepatotoxicity, possibly via inhibition of oxidative stress, inflammation, and apoptosis (Rashid et al., 2020).

7.4. Nervous system

Increasing evidence demonstrated that cisplatin could cross the blood-brain barrier and cause central nervous system injury (Andres, Gong, Di, & Bota, 2014). Fortunately, some studies showed that PM ethanolic extract at 100 and 200 mg/kg attenuated cisplatin-induced oxidative stress in the cerebral cortex via its antioxidant activity (Ridzuan et al., 2019). In other words, PM ethanol extract can alleviate drug damage to the central nervous system. Besides, when there is injury or damage to the central nervous system, it can disrupt the normal functioning of these cognitive processes and lead to the development of cognitive impairment (Greenhalgh, David, & Bennett, 2020; Walker & Tesco, 2013) Cognitive impairment is sometimes neglected but common, which has a profound effect on the daily life of patients (Romo-Araiza & Ibarra, 2020). Evidence shows that patients with mild cognitive impairment have a far higher rate of developing chronic neurodegenerative diseases than cognitively normal persons (Goldman et al., 2018). Meanwhile, available medications merely slow the decline process but cannot reverse it (Sun, Ho, Zhang, Hong, & Zhang, 2023). Thus, alternative treatment approaches for mitigating cognitive impairment are greatly needed.

George, Ng et al. found that PM exhibited antioxidant and anticholinesterase activity, contributing to enhanced cognition *in vivo*. The results suggested that the extract possesses neuroprotective properties (George, Ng, et al., 2014). More than that, several studies have indicated that PM has positive effects on cognitive status and mood. The bioactive compounds present in PM may have neuroprotective effects, although there is still a lack of human studies examining the connection between PM consumption and cognitive status (You, Shahar, Haron, & Mastura Yahya, 2018). Additionally, according to reports, the supplementation of PM extract for six months can notably significantly improve visuospatial memory, reduce tension, anger, confusion, total negative subscales, triglyceride levels, and increase brain-derived neurotrophic factor levels in older adults with Mild Cognitive Impairment (Lau et al., 2020). Christapher et al. investigated the use of PM alleviated both paclitaxel- and scopolamine-induced neuropathic pain and cognitive impairments, showing a dose-dependent effect. A potential mechanism is PM exhibits potential neuroprotective effects attributed to its antioxidant properties, inhibition of lipid peroxidation, and regulation of cholinergic neurotransmitter functions (P. V. Christapher, Muthuraman, Zhang, Jordon, & Jonathan, 2021).

The findings of Yahya et al. indicated that PM supplementation could improve mood and quality of life, and participants did not report any adverse effects after six weeks of supplementation (H. M. Yahya et al., 2017). In addition, Bashir and colleagues evaluated the effects of PM extract on chronic ultra-mild stress-induced anorexia and anhedonia. Chronic administration of PM extract was found to reduce anorexia and improve anhedonia among stressed mice (Bashir, Aziz, & Noor, 2022a). Meanwhile, they suggested that the PM aqueous extract has antidepressant effects, as evidenced by reduced immobility time, enhanced spatial memory, decreased corticosterone levels, increased brain-derived neurotrophic factor levels, and lowered monoamine oxidase-A enzyme levels, leading to increased levels of monoamines (serotonin and norepinephrine) in the hippocampus (Bashir, Aziz, & Noor, 2022b). Besides, they explored the effects of PM aqueous effects on Kruppel-like factor11 and Sirtuin1 levels in the hippocampus of stressed mice. The results showed that PM aqueous extract treatment showed a significant reverse in an elevated level of Kruppel-likefactor11 and Sirtuin1 in the hippocampus of stressed mice after treatment of 8 weeks (Bashir, Aziz, & Noor, 2022c). In another study, leaves of PM standardized extract, 1 and 100 mg/L, were used to evaluate the anti-stress effect in the chronic unpredictable stress zebrafish model. Both concentrations showed ameliorating effects only in the exploratory test. No significant changes were detected in the treatment groups. Cortisol analysis showed that after four days, the chronic unpredictable stress effect still affected the zebrafish Hypothalamus–Pituitary–Adrenal axis, but PM extract and fluoxetine treatment might need a more prolonged duration treatment to give the desired effect (Rahim et al., 2022). Moreover, the leaf component of PM has demonstrated significant potential as a future antidepressant option. This is attributed to the presence of flavonoids, particularly those involved in memory enhancement and the elevation of neurotransmitter levels in the brain, as reported. The current research observations suggest that conducting experimental screening for the antidepressant activity of the leaf part of PM is highly recommended (Bashir et al., 2020).

Chronic depressive disorder or clinical depression has become a highly prevalent mental disorder affecting over 300 million populations worldwide (Haenisch & Bönisch, 2011; James et al., 2018). Natural medicinal plants and healthy food are considered alternative therapies to control the progression of depression and depressive-like symptoms with few side effects (Yeung et al., 2014). Many natural compounds, such as caffeine, green tea catechins, anthocyanins, ginsenosides, and resveratrol, are potential therapeutic agents with antidepressant-like bioactivities (A. Kang et al., 2017; Mao et al., 2020; Nabavi, Daglia, Braidy, & Nabavi, 2017).

7.5. *Cardiovascular system*

Cardiovascular diseases (CVDs), a major cause of global mortality (Liao et al., 2023), are primarily fueled by hyperlipidemia, a substantial risk factor for CVDs (Karr, 2017; Prabhakaran et al., 2018). Christapher, Vikneswaran, et al. (2015) investigated results that revealed the antihyperlipidemic effect of leaves of PM in an acute hyperlipidemic rat model. The study also suggested that the methanol extract possesses a higher antihyperlipidemic effect than the aqueous extract (Christapher, Vikneswaran, et al., 2015). Besides, another significant risk factor for CVDs, hypertension, is also severely threatening human health (Castilla-Guerra, 2022; Gumprecht, Domek, Lip, & Shantsila, 2019; Suvila & Niiranen, 2022). Khalid & Salam found that Malaysian tropical plants, especially PM, are potential sources of natural antioxidant and antihypertensive agents (Khalid & Salam, 2018).

Upon chronic exposure, cadmium can accumulate in other body parts, including the heart and aorta, leading to various diseases (Tai et al., 2022). Kusumaningrum et al. (2019) demonstrated that PM leaves ethanol extract could protect the aortic wall against cadmium chloride exposure in mice. Afterward, they conducted another study to investigate the protective effect of PM leaf extract on the histopathological changes in the aorta wall in mice induced by cadmium chloride. The result showed PM leaf extract could protect mice's aorta walls from the damaging effect of cadmium chloride, with the optimum dose being 400 mg/kg bw (Kusumaningrum et al., 2020).

7.6. *Urinary system*

The kidney plays a pivotal role in eliminating toxic metabolites and is susceptible to toxicity induced by xenobiotics (Hassanen, Fahmi, Shams-Eldin, & Abdur-Rahman, 2020). Acute kidney injury, often caused by drugs, not only increases mortality and morbidity but also prolongs hospital stays, diminishing quality of life (Yu et al., 2021). For instance, cisplatin can cause severe deterioration in kidney function (Khan et al., 2013). The findings of Michael and his team revealed that PM leaf methanol extract had the ability to decrease urea and creatinine concentrations, suggesting its potential to mitigate the side effects of the chemotherapy agent cisplatin (Michael & Isnindar, 2013). Other researchers further studied and found the effective dose of PM leaf methanol fraction, which demonstrated nephroprotective activity in cisplatin-induced rats was 4.547 mg/200 g bw (Rita, Kusharyanti, & Wahdaningsih, 2013). Not only that, it has been proved that 1308 mg/200 g bw of PM leaves n-hexane extract decreased kidney damage and urea and creatinine levels, which indicates that it has the potency to reduce the side effects of chemotherapy agent cisplatin (Tommy, 2013). Kidneys are the first target site for heavy metal (mercury) deposits and toxicity (Vieira et al., 2021). The protective effect of PM leaf extract on the histopathological changes of kidneys induced by mercuric chloride in mice was investigated by Aprianti, Widiyatno, and Sudjarwo (2017). Their results showed that PM leaf extract could protect mice kidneys from the damaging effect of mercuric chloride, with the best dose of PM 400 mg/kg bw (Aprianti et al., 2017).

7.7. Reproductive system

Mercury chloride causes harmful effects on the liver, blood, kidneys, and the male reproductive system (Apaydin, Baş, Kalender, & Kalender, 2016; Uzunhisarcikli, Aslanturk, Kalender, Apaydin, & Bas, 2016). It induces various pathological processes and membrane damage, ultimately resulting in the loss of sperm motility (Agarwal, Saleh, & Bedaiwy, 2003; Vachhrajani K.D. et al., 1988). Zulfar (2017) demonstrated that the ethanol extract of PM leaves can act as a preventive measure against the toxic effects of mercury chloride on the thickness of seminiferous tubule epithelium and the count of spermatocytes. The group treated with 200 mg/kg bw of PM ethanol extract exhibited the most favorable results (Zulfar, 2017).

Cadmium has been shown to lower testosterone and steroidogenic enzyme levels, and decrease sperm concentration and viability, ultimately disrupting the fertilization process (de Angelis et al., 2017; Hernández-Rodríguez et al., 2016). The findings of Siswanto suggested that PM leaves ethanol extract could shield the spermatogenic cells in the testes of mice from the harmful effects of cadmium chloride, with the optimal dose being 400 mg/kg bw (Siswanto, 2018).

The potential of certain substances to enhance sexual behavior has prompted studies on aphrodisiacs derived from plants (Melnyk & Marcone, 2011). Udani et al. revealed that supplementing with PM and the proprietary *Eurycoma longifolia* extract, Physta, for twelve weeks was well-tolerated and more effective than a placebo in improving sexual performance in healthy volunteers (Udani et al., 2014).

7.8. Immune system

A disturbance in the components of the immune system leads to the development of various health problems (Brindha & Pavelic, 2016). Hence, it is of great significance to search for an immunomodulatory agent that affects the immune system (Chen et al., 2022). Recently, natural substances have been attracting increased attention owing to their multiple biological activities, including immunomodulation (Qin et al., 2022; Xie, Huang, Meng, Shi, & Xie, 2022). George, Chinnappan, Choudhary, Bommu, and Sridhar (2014) investigated the immune system-modulating characteristics of PM aqueous extract on Swiss albino mice through the carbon clearance assay. The extract demonstrated a notable enhancement in phagocytosis at doses of 200 and 400 mg/kg bw (George, Chinnappan, et al., 2014).

Furthermore, Herpes simplex virus type 1 (HSV-1) employed several strategies to evade the host's immune system, allowing it to establish latent infections and periodically reactivate (Verzosa et al., 2021). Therefore, there is an increasing need to find new antiviral compounds where pure compounds of plant origin have been shown to possess antiviral activity against HSV types (El-Toumy et al., 2018).Shahar et al. found that aqueous extract of PM could be a potential candidate for anti-HSV-1 activity (Shahar, Hamdan, Baba, & Paul Joko, 2015). Indeed, further studies are required before a conclusive experimental finding is suggested.

Based on these above observations, it is evident that PM is a plant with various bioactive compounds that have the potential for medicinal properties and are effective in combating and treating common illnesses. Numerous *in vitro* and *in vivo* studies have demonstrated the other therapeutic activities of PM against body systems diseases, sexual performance and well-being, cognitive function and mood, and microbial infections.

8. Application of nanotechnology in PM

The tremendous progress of nanotechnology and nanomedicine has brought a variety of opportunities to the development of nanomedicines, which are extensively exploited to ameliorate the solubility of insoluble drugs (Hu, Johnston, & Williams, 2004) and to achieve sustained drug release (Kamaly, Yameen, Wu, & Farokhzad, 2016; Peng et al., 2013), long-circulating and targeted delivery (Moghimi, Hunter, & Murray, 2001), and spatial-temporally controllable drug release (D. Huang et al., 2020; Y. Wu, Wang, Huang, Yang, & Wang, 2017). Application of nanotechnology in the synthesis of plant material, especially in functional properties, is expected to improve solubility and bioavailability, protect from toxicity, enhance pharmacological activity, enhance stability, improve tissue macrophage distribution, and protect from physical and chemical degradation (Nadzirah et al., 2014). Likewise, PM has been studied and prepared into various nanoparticles due to its wide range of uses and activities (Fig. 10).

8.1. PM extract-loaded gold nanoparticles

Gold nanoparticles (AuNPs) have been applied as an antimicrobial agent, cancer therapy, and diagnostic tools in fluorescence tomography, among others (Firdhouse & Lalitha, 2022; Murphy et al., 2008; Sardar, Funston, Mulvaney, & Murray, 2009; Wei, Famouri, Carroll, Lee, & Famouri, 2013; P. Zhao, Li, & Astruc, 2013). Initially, Borhamdin, Shamsuddin, and Alizadeh (2014) presented a bioinspired method for synthesizing magnetically recoverable AuNPs catalysts on a Fe_3O_4@-SiO_2 support. Subsequently, they investigated an environmentally friendly method for synthesizing AuNPs using an aqueous leaf extract of PM. This biosynthesis is simple, time-saving, and eco-friendly, requiring only 20 min to produce AuNPs with an average particle size of 23 nm (Borhamdin et al., 2014). The newly prepared biostabilized icosahedral AuNPs exhibited good catalytic activity in reducing 4-nitrophenol to 4-aminophenol (Borhamdin, Shamsuddin, & Alizadeh, 2015).

8.2. PM extract-loaded silver nanoparticles

Silver nanoparticles (AgNPs) have been widely studied in various scientific applications due to their unique physicochemical and biological features. These include ease of functionalization or connection with different ligands for customized properties, antimicrobial toxicity, effective cytotoxicity against cancer cells, catalytic applications, and more (Akter et al., 2018; Jain, Huang, El-Sayed, & El-Sayed, 2008).

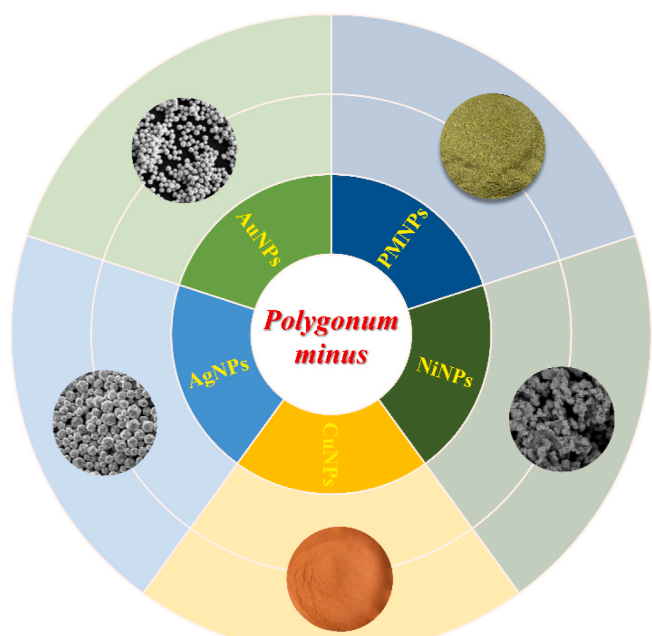

Fig. 10. Various PM nanoparticles. AuNPs, PM extract-loaded gold nanoparticles; AgNPs, PM extract-loaded silver nanoparticles; CuNPs, PM extract-loaded copper nanoparticles; NiNPs, PM extract-loaded nickel nanoparticles; PMNPs, nano-size PM powder. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

Ullah et al. introduced a method using aqueous IL and microwave extraction to extract lignocellulosic biomass from PM. They achieved a high yield of nanoparticles using recycled ILs (Ullah, Wilfred, & Shaharun, 2017). Additionally, the PM plant extract was employed in the synthesis of AgNPs from a silver nitrate solution. The initially colorless mixture gradually transformed from yellowish-green to reddish-brown, indicating the reduction of silver ions ($Ag+$) over several minutes. Three types of bacteria—*Staphylococcus aureus, Escherichia coli, and Pseudomonas aeruginosa*—were selected for testing. Morphological changes in bacterial cells treated with AgNPs were observed using a field emission scanning electron microscope (FESEM), revealing the excellent antimicrobial properties of AgNPs against these microorganisms (Nadzirah, Mahamudin, Muhamad, & Latif Ibrahim, 2019). In a different investigation, Kamarudin and colleagues established an environmentally friendly method for producing ultrafine and well-defined spherical AgNPs (5–20 nm) using an IL. The extract from PM leaves served as both a green reducing agent and a capping agent in the synthesis process. The findings indicated that the IL and phenolic compounds worked synergistically to reduce Ag + to AgNPs and stabilize the nanoparticles (Kamarudin et al., 2022).

8.3. PM extract-loaded copper, nickel nanoparticles

Ullah and the team (2018a) showed that bioactive compounds from PM can be extracted using an IL-based microwave-assisted method. The obtained extract was then employed to produce copper nanoparticles (CuNPs). UV/Vis results showed that this synthesis was fast, well dispersed, and nanosized CuNPs in comparison to conventional synthesis. Moreover, the antibacterial activity of the synthesized CuNPs exhibited an effective inhibitory zone against three different bacteria, namely *Staphylococcus aureus, Escherichia coli, and Pseudomonas aeruginosa* (Ullah, Wilfred, & Shaharun, 2018a). Ullah and the team (2018b) performed an additional experiment to extract bioactive compounds from PM using 1-ethyl-3-methyl imidazolium chloride along with ultrasonication. The resulting extract was utilized to create nickel nanoparticles (NiNPs). The synthesized NiNPs demonstrated high effectiveness against three different bacteria—*Aeromonas hydrophila, Escherichia coli, and Staphylococcus aureus*—in disc diffusion tests at various concentrations (Ullah, Wilfred, & Shaharun, 2018b).

8.4. Nano-size PM powder

The recently developed superfine grinding technology as a useful tool for preparing super fine powder has opened a vast area of research and development for the medicinal benefits of natural food products (Archana, Aman, Singh, Kr, & Jabeen, 2021). This approach has the potential to enhance surface area, thereby improving bioavailability, distribution, and absorption (Xiaoyan, Yang, Gai, & Yang, 2009; Ya Ling, Sheu, Lee, & Chau, 2008). Additionally, it contributes to improved dispersibility, solubility, and water-holding capacity (Ramachandraiah & Chin, 2016). Nadzirah et al. utilized a planetary ball mill to reduce the particle sizes of PM powder efficiently, achieving a successful preparation at the nanoscale (Nadzirah, Rusop, & Latif, 2015a). Afterward, the same team explored the changes in the physical properties of PM resulting from the grinding effect. The planetary ball mill successfully reduced the particle size of PM to the range of 227 nm–241 nm. FESEM images demonstrated significant alterations in particle size morphology, featuring a higher degree of cell breakage attributed to the planetary ball mill process. Atomic force microscopy results indicated changes in particle roughness due to the grinding process. Furthermore, energy-dispersive X-ray analysis revealed that the sample exhibited the highest elements of carbon and oxygen, averaging 86%, suggesting the presence of carbohydrates (Nadzirah, Rusop, & Latif, 2015b).

9. Conclusion and future perspectives

PM is an aromatic plant that has gained popularity owing to its excellent nutritional value. It is extensively used for nutritional and medicinal purposes. Despite the usage of PM in food and herbal medicine in countries like Malaysia and India, limited information is available about its therapeutics and pharmacology. Notably, extremely few articles were found on the application potential of this species, with particular reference to its applications in the food, agricultural, medicinal, and nanotechnology fields. This review discusses the above-said issues in detail and in a scientific manner that could be beneficial for the scientific community for the development of PM applications for the benefit of society. However, there are still some problems to be solved in the later application of PM.

First of all, the variability of the composition profile, amounts of individual components, and yield of the extract from the PM materials is due to the influence of different factors. Therefore, selecting the best parts and most effective methods of extracting from PM is essential to preserve the quality and achieve maximum effect.

Second, most of the studies observed positive effects on the characteristics of products like meat, vegetables, and fruits after the addition of PM extracts by controlling the quality deterioration (microbial growth inhibition, antioxidant activity, and preservation of sensory properties). Besides the promising results obtained from the literature, there is much to achieve concerning product quality, shelf life, and consumer acceptance of PM extract-based additives and films on food products. For example, PM extract-based biodegradable films are lacking in the market because there are still obstacles to using sustainable polymers instead of synthetic ones. For this reason, more detailed studies must be done to improve the properties of the additives, films, and coatings for the industrial application of food since the improvement of some material characteristics is generally associated with a decrease in others.

Third, although PM powder/extract has been applied to test all types of animals, some challenges still need to be solved for large-scale feed production. Life cycle assessment of animal feed production using PM should be further investigated for better environmental impact, particularly in the livestock, poultry, and aquaculture industries. In order to maximize the quantity and quality of extracted nutritive values and secondary metabolites in PM, each process, such as drying methods, extraction techniques, and analytical methods, should be optimized. This information can help feed formulators fully exploit the presence of nutritional value and secondary metabolites in PM when devising diets for animals.

Fourth, although insights have been revealed about the pharmacology properties of PM, some gaps between basic studies and clinical application still exist, which limits the use of PM for body disease clinical treatment to a certain extent. Therapeutic and safe doses of active ingredients from PM need to be established based on recent pharmacological and pharmacokinetic trials in nonclinical or clinical settings. At the same time, studies in which the ingredients of PM are extracted and then applied to simultaneously explore the suitable cellular, animal, and clinical levels are lacking.

Finally, nanoparticle biosynthesis by PM is eco-friendly, easy to access, non-toxic, and cost-effective, and it enhances the therapeutic efficacy of herbal drugs. These delivery systems ensure the delivery of plant bio-actives to the targeted site, such as the liver, brain, heart, kidney, etc., with low doses in contrast with conventional plant extracts or phytomolecules. However, despite PM applications in nanotechnology providing enough information, they are not enough. On the one hand, studies are required to explore the mechanism and pathways PM uses through the biosynthesis of nanoparticles. On the other hand, there are still possibilities for the development of new carriers in order to reduce the toxicity and enhance the therapeutic efficacy of herbal drugs. Meanwhile, the factors and conditions of the PM-based NP synthesis need to be developed on a large scale to be suitable for commercial production. Besides, various fields and applications need to study the impact of PM-NPs.

In addition to the discussed fields, strategic exploration of the understanding and application of PM using biotechnology may be a good approach. These methods aim to optimize the production and utilization of PM bioactive compounds for various fields. Such as metabolic pathways in PM can be improved through genetic engineering to increase the yield and consistency of bioactive compounds. Targeted genetic modification can produce PM varieties with higher therapeutic efficacy and improved nutritional status. In addition, using genomics, proteomics, and metabolomics can provide a comprehensive understanding of the molecular mechanisms behind various PM applications. This information can guide the development of improved extraction methods, and application strategies.

In general, PM and its main bioactive compounds have enormous application potential and represent potential candidates for food, feed, and medicine. Future research is urgently required to exploit of this promising resource with efficient green protocols, and additional alternative uses should also be investigated to facilitate the overall value-added aspect of this vital herb.

CRediT authorship contribution statement

Zhongming Yang: Writing – original draft. **Xi Deng:** Writing – original draft. **Zhongguo Yang:** Writing – original draft. **Mingzhao Han:** Writing – original draft. **Norsharina Ismail:** Writing – review & editing, Funding acquisition, Conceptualization. **Kim Wei Chan:** Writing – review & editing. **Ahmad Faizal Abdull Razis:** Writing – review & editing. **Norhaizan Mohd Esa:** Writing – review & editing. **Ket Li Ho:** Writing – review & editing. **Md Zuki Abu Bakar:** Funding acquisition, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

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Glossary

PM	*Polygonum minus*
bw	body weight
GC-MS	gas chromatography–mass spectrometry
SPME	Solid Phase Microextraction
TPC	total phenolic content
TFC	total flavonoid content
TP	total phenolic
TF	total flavonoid
FRAP	ferric reducing antioxidant power
DPPH	2,2-diphenyl-1-picrylhydrazyl
IL	ionic liquid
ILs	ionic liquids
PV	peroxide value
TBA	thiobarbituric acid
FFA	free fatty acid
PLA	polylactic acid
PBS	polybutylene succinate
CLE	curry leaf extract
AST	aspartate aminotransferase
ALT	alanine aminotransferase
CVDs	cardiovascular diseases
MIC	minimal inhibitory concentrations
MBC	minimal bactericidal concentration
HSV-1	herpes simplex virus 1
AuNPs	gold nanoparticles
AgNPs	silver nanoparticles
Ag^+	silver ions
FESEM	field emission scanning electron microscope
CuNPs	copper nanoparticles
NiNPs	nickel nanoparticles
NPs	nanoparticles

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